ماجستير تناسليه (5)

Infertility

(Male Infertility)

د/هانى ابوالوفا

2017

د. مسلم

just print

01025329200- 0502200362

"Male Infertility"

Def.: Failure of Conception For at least 12 months of unprotected regular sexual intercourse.

Frequency

USA

"of Couples"

15% are infertile (meet this definition):

- 35% → ♀ Etiology
- 30% → ♂ "
- 20% → Combined
- 15% → unexplained.

≃(90%) of Cases are d.t:

- low sperm Count,
- Poor quality or Both. (Motility, Morphology)

(without tt)

- 23% Conceive within 2 Ys
- 10% Conceive ē in 4 Ys
- & pts. ē severe oligo (< 2 million/ml) → 7.6% of them Conceive ē in 2 Ys.

Internationally:

- Highest Fertility rate → Finland.
- Lowest " " → UK

] d.t { genetic, environmental, social habits.

- Sperm Count: in "21st"
  - 1940 → 113 mil/ml
  - 1990 → 66 mil/ml.

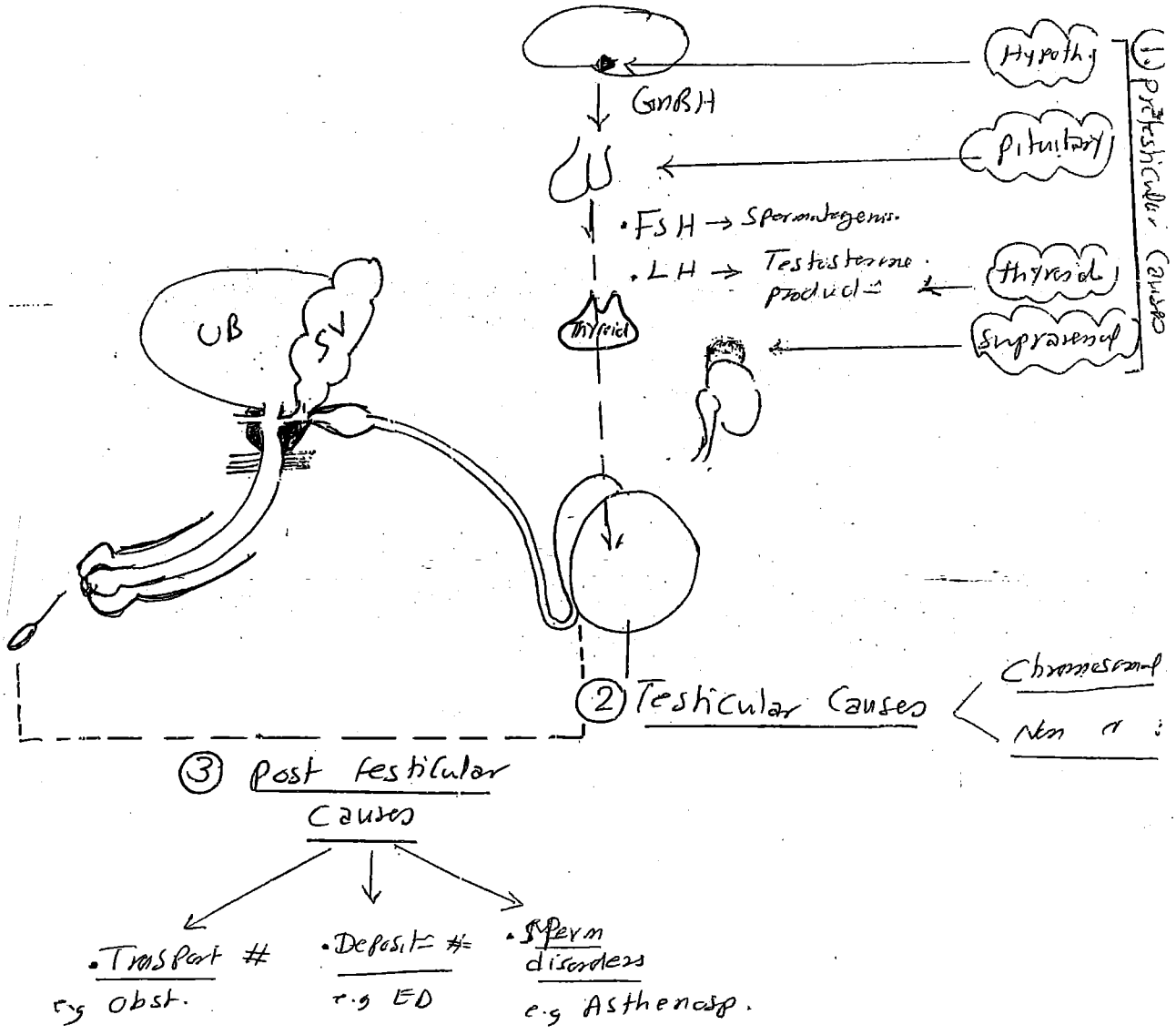
] d.t { env. Conditions & Toxins, difference in Lab / geographic.

Age:

- Fertility → ↓ ē Aging (See effect of Aging on Testicular Function)

Causes of Male Infertility

- **Pretesticular** (Endocrinal Infertility).
  - ✓ Hypothalamic causes
  - ✓ Pituitary causes
  - ✓ Peripheral organs causes. (Thyroid, Suprarenal)
- **Testicular**
  - Chromosomal
  - Non Chromosomal
- **Post-testicular**
  - Transport disorder e.g. Obstruct
  - deposit disord e.g. ED, PE
  - Motility disorc e.g. Asthenozo.



• Pretesticular Causes of infertility
(Endocrinal infertility)

Hypothalamic-pituit. axis Interruption.

↓

Hypothalamic Causes.

- Kallman Synd
- Prader-Willi Synd.
- Idiopathic HH (IHH)
- Other Causes.

Pituitary Causes.

- Pan-Hypopituitarism
- Isolated FSH deficency.
- " LH N.
- Hyperprolactinemia
- Hemochromatosis.
- Pituit. Cushing (↑ Cortisol)

Peripheral organ Causes.

- Adrenal disorders (Cortical < Excess / deficiency)
- Thyroid N (Hypo & Hyper)
- Estrogen Excess.

Hypothalamic Causes

1. Kallman Synd.:

- Def → Isolated GnRH deficiency (either < partial or complete).
- Genetic Transmission:
  - AD (6%) (FGFR1)
  - AR (25%)
  - XR (10%) (KAL1 Mutation)
- Incid: 1:10,000 - 60,000 live births
- Sex: M:F = 5:1
- Pathophysiology: → Mutation in KALIG1 (Kallman Interval Gene-1).

(Function: Guide The Transmission of Neurones From olfactory area to Hypothalamus & olfactory bulb during Intra uterine period)

↓

Failed Migration

↓

① Failed GnRH secretion → Hypogonadism

② Failed Formation of olfactory bulb → Anosmia. (Nose)

- CIP ① Hypogonadism:
  - include 3: Failed Puberty (Eunuchoid features), Sexual dysf., Infertility.

② Anosmia (Cardinal features & should be tested).

③ Midline defects: cleft lip & palate.

④ other features:
- CVS
- UT
- Neuropsychiatric
- Skin → Hypopigm. & Ichthyosis.

(Abnormalities.)

* Color Blindness
* obesity

CIP

1. Hypogonadism: تشمل الرجال والبنات ← Failed Puberty, Sexual dysf., Infertility.

CIP

A Failed Puberty (Eunuchoid Features):

① Body proportions: (مهم)

1. upper segment (Crown to pubis) : lower segment (Pubis to Heel)
   < 1 (CNLLY at 3y/7y: 1.7 / 1.3 / 1)

2. Span > Height. (CNLL: equal)
   - distance bet outstretched arms

(2 Exceptions ??)

② 2ry Sex Ch:

- Hair — Sparse facial & body Hair
  - lack of Temporal Recession
  - Female pattern of Pubic Hair: before
- High pitched Voice
- Obesity → Female pattern distribution of Body Fat (Hip & Trunk).

- ↓ Ms mass & strength.
- Gynaecomastia.

③ Sex organs:

- Testes — Small, Firm ± Cryptorchism
- penis: micropenis
- scrotum: Hypopigmented & under developed.

B Sexual dysf: ↓ Libido, ED.

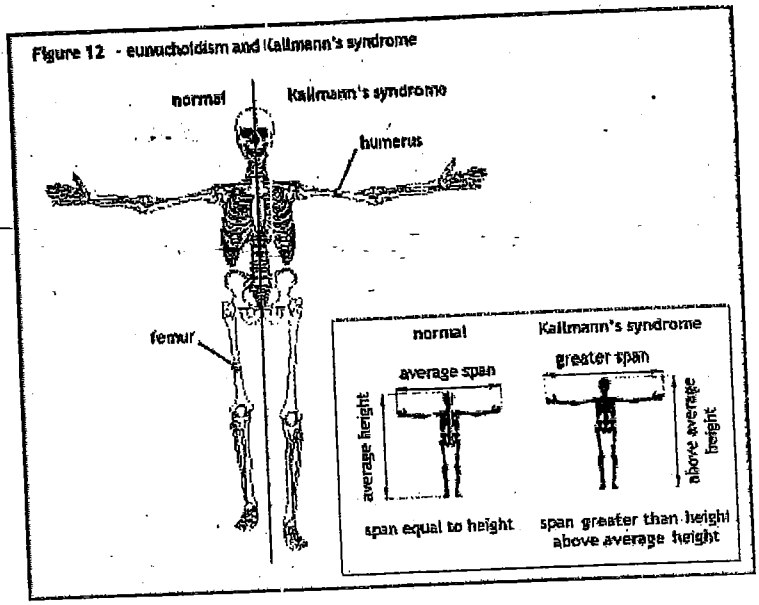
B Infertility:

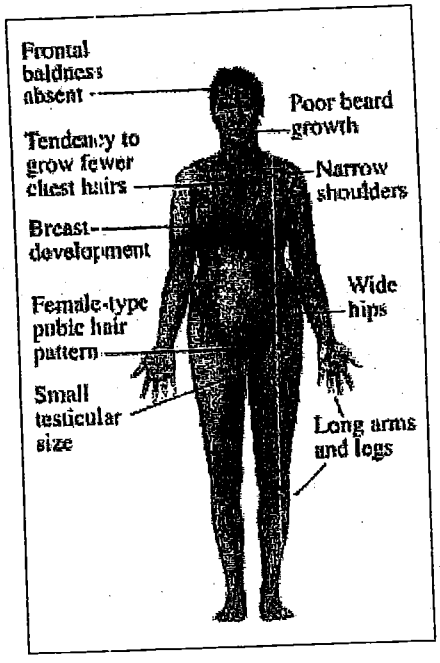
- FSH & LH → low NL (or) ↓↓
- Testosterone: very ↓↓ (Total & Free)
- Semen Analysis:
  - Azoo or
  - Severe oligo.
- Testicular Biopsy:
  - pre pubertal Testes.

Imaging Studies.

- US < Testicular / Renal
- MRI: → abn L olfactory bu
- Bone densitometry (لكل Hypogonadism)

Eunuchoidism





- DD
  1. Hypergonadotropic (LRP) Hypog. → ↑ FSH & LH
  2. Constitutional delayed puberty : (CDP)
     - No (anosmia, midline defects)
     - Chlorpromazine challenge:
       Test → ↑ PRL → in CDP
       No Response → in True. failed puberty (KS)
  3. IHH : No (as CDP).

- NB : to differentiate bet. Hypothalmic & pituitary Cases of Hypogonadism:

GnRH test

↑ FSH & LH → Hypothalamic Aet.

No Change in FSH & LH level → Pituitary cause

Methodology

✗ Single Parenteral Method → Periodic S.C or IV 100 µg GnRH → Venous sampling at: 15, 30, 45 min. → NLLY: LH: 2-5 Fold ↑ / FSH: 1.5 fold ↑

✓ Periodic Pump method → S.C 5 µg GnRH for 7 ds every 90 - 120 min. (by portable mini pump)

NB If Periodic test is -ve & still suspect Hypothalamic AET → Pump test for 7 ds then Periodic test.

Treatment
(aim)

Induction of Puberty
(لو مش متزوج)

ليه لازم نعمل البلوغ ؟؟

aim:

1. Psychological (sense of wellbeing)
2. ↑ penile size ...
3. prevent osteoporosis

(not improved later on by T. replacement) (لازم نعالج وقت البلوغ)

BY

Androgen Replacement therapy for life.

(parentral or Transdermal)

NB: Follow up & Rx Measures: (قاعدة "شفوي")

1. Prostate < Exam & PSA
2. Hematocrite Value
3. Lipid profile
4. Bone Age Assement.
5. T. & Estradiol level

سؤال: هل تنفع لولادة انابيب الاجنة ؟؟

- hMG.
- Testosterone ??

hMG & hCG لازم

Induction of Fertility
(لو هايتزوج)

(Spermatogenesis)

[after Marriage]

either BY: (غالي جدا)

GnRH

5-20 μg Every 90-120 min. (كل ساعتين)

S.C BY the portable pump.

(but its cumbersome nature → reserved for those failed hCG & hMG Rx.) (دائري) (مع)

- Correspond to LH
- Dose: 1000-3000 IU 2-3 Times/weekly (IM)
- ع السوق:
  - Pregnyl (5000)
  - Profasi (N)
  - Choragon.

Combined hCG & hMG (menotropin)

- Correspond to FSH
- Dose: 75-150 IU 2-3 times/w (IM)
- ع السوق:
  - Pergonal
  - Humegon

till

appearance of sperm &/or occurance of pregnancy.

NB:
- Combined Rx may be Needed for 1-2 Ys specially: Resistant Cases.
- Sperms may appear within
  1. 3-6 ms (in Combin.)
  2. 6-24 ms (in GnRH)

peak T after 24 ms

NB * ttt by GnRH is effective or Combined hCG & hMG.

* the advantage of ttt by GnRH or GnsH is that: intiation of spermatogenesis & puberty occurs at the same time.

* induction of puberty by Androgen replacement therapy occurs as following:

  * we give Testosterone enanthate e.g Depotestone or Cidotestone 250 mg 1 ampoul IM as following:

    - 1st Year: → 1/8 أمبول كل ٦ أسابيع
    - 2nd Year: → 1/4 أمبول كل ٤ أسابيع
    - 3rd Year: → أمبول كل ٢ أسبوعين

* Androgen therapy will not disturb the future fertility when Gn or GnRH is given to intiate spermatogenesis.

"Androgen therapy" (المسرع)
↓
Given either BY

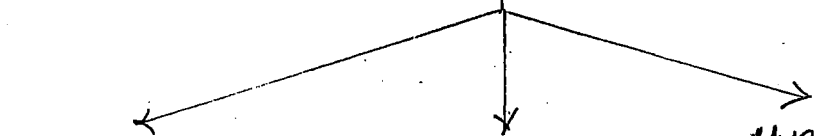
1. IM injection: Testosterone Enanthate 250 mg IM
2. Testosterone implant: 400 – 600 mg Twice yearly
3. oral tab:
   - Alkylating forms X d.t hepatic toxicity.
   - Andriol (Test. Undecanoate): 120 – 170 mg/d
   - Proviron or Provimest (Mesterolone): 50–75 mg/d

(ad) * S.E of HCG: ① down regulation of Receptors.
② Abs formation that can block HCG action.

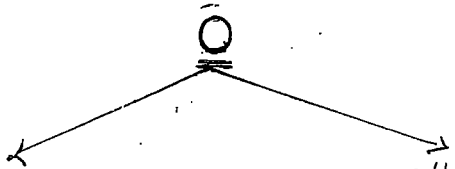
Prader - Willi Synd

=

(H3O Synd)



- **Hypotonia**
  - Severe, generalized, at birth → feeding difficulties.
- **Hypomentia (MR)**
- **Hypo-gonadism** (See before)



- **Obesity**
  - d.t ↑ appetite → Hyperphagia → difficult to be controlled.
- **Others:**
  - Cryptorchidism
  - Hypopigm.
  - DM.
  - ± GH deficiency

- Incid : 1:10.000
- AET : defect or deletions of paternally derived Chromosome arm (15q11-13) → ↓ GnRH.

NB: **Laurance Moon Biedl Synd.** (Was previously considered as Hypothalamic disorder but now proved incorrect).

- Hypogonadism
- MR
- Retinitis Pigmentosa
- Poly-dactyly

Idiopathic HH (IHH).

- Failed GnRH with No detectable Cause (Isolated)
- How to differentiate bet it & K-S?

May be d.t Genetic defects

- No Anosmia
- No midline defects
- No + FH.

- FGFR,
- FGF8
- Chromodomain-Helicase (DNA binding protein 7.

- HH → as in K.S

Other Causes

"Ferritin ↑ in all cases of Acq. HH"

1. Tms -

2. Granulomas
   - TB
   - Sarcoidosis
   - & Hemochromatosis [Most common cause of Acq. Hypog.]

3. Fracture Skull Base
   - Ischemia
   - Hge
   - Radiat- &
   - Metastasis.

4. Malnutriton:
   - malabs.
   - Tm. Cachexia
   - Anorexia Nervosa (HH Reversible that improves ↑ w.t).
   - Chr. diseases ✓
     - CRF
     - Sickle Cell anemia.

diencephalon Tm:
- Craniopharyngioma
- Meningioma
- Metastases

dez. Non functioning

Cong. malformation or Tm that's present at birth & ↑↑ gradually

- origin: remenants of "Rathke pouch" [depression on Roof of developing Mouth & Embryo gives rise ant pituit]
- Site: Suprasellar Region
- Effect: Compression of pituitary stalk → ↓ PIF → ↑ PRL
- CIP ① Commonest presentat^: (↑ ICT) ✓
  ② may be: ↑ PRL.

• Pituitary Causes of Infertility

① Panhypopituitarism

- AEt
  - Trauma
  - Tm
  - Granuloma
  - Infarction
  - Iatrogenic (during surgery)
  - Genetic Mutation (rare)

Pituit. deficiency is to be expected if > 75% of Pituitary tissue is destroyed.

CIP

Prepubertal Panhypopituitarism

↓FSH & LH → • Hypogonadism e.g. Failed puberty

- DI (↓ ADH) (↑ Thirst & Polyuria)
- ↓ GH (Dwarfism)
- ↓ TSH (Hypothyroidism)
- ↓ ACTH (Addison)

NB. Testes: < Firm Small.

- because GH is low → Eunuchoid tall Stature Not seen.

Post pubertal Panhypo.

- Lost pubertal marks
- Sexual disorders
  - ↓ libido
  - ED
- Infertility

NB: Testes are < Small Soft.

Hx

[1] Hx of Aetiology e.g. Surgical removal of Tm.

[2] Replacement of missing Hormones:

- hCG / hMG Combined Hx
- Cortisol, GH, Thyroid Hs & Test.

NB GH Replacement may be needed d.t:

- Before puberty → to stimulate growth
- After puberty → For initiation of spermatogenesis by improving (FSH) action.

2-3 Isolated deficiency

Isolated LH deficiency (Fertile Eunuch Synd = Pasqualini Synd)

This disorder CH BY:

① Partial ↓ either in < amount or Activity of LH.

② The amount is sufficient to induce Spermatogenesis (so he is fertile) but insufficient to induce virilization (so he is Eunuchoid).

- The pt will show:
  - FSH: NL
  - LH & T: Low NL.
- Biopsy:
  - Spermatogenesis ✓
  - Leydig cell Atrophy ✓

Isolated FSH deficiency

↓ FSH with NL LH

↓

NL Verilization (puberty) but defective Spermatogenesis (infertility).

- AEt. of both dis. ± d.t:
  - [1] Hypothalamic dysregulation e.g
    - Genetic
    - [2] Mutation in β subunit of LH & FSH Gene.
    - Proved by improvem of FSH & LH Sec. by GnRH administration
- HI → Replacement therapy:
  - LH by hMG
  - FSH " hMG.

4. Hyperprolactinemia

- Pathophysiology:
  - PRL Hormones is 198 aa protein (23-KD) produced in the Lactotroph Cells of Ant. pituitary

Regulation of PRL Secretion

Inhibitors of PRL Secretion (PIF)

- Dopamine: Neurotransmitter produced by Hypothalamus acts on D2 Receptors of the Lactroph cells → ↓ PRL Secretion
- So may be Named: "PIF"
- So: any Cause ↓ PIF will → ↑ PRL.

Stimulators of PRL Secretion (PRF)

- TRH
- Estrogen
- VIP (Vaso active intest peptide) ← Hormone in Gut, Pancreas, Hypothalamus
  → ++ PRL secretion
- So may be Called: PRFs (Prolactin releasing factors)

- Secretion of PRL is (Pulsatile)
- PRL Sec. ↑↑ by: (usually < 50)
  - Exercise
  - Sleep
  - Stress < Physical / Psychological
  - ♀ Pregnancy
  - Chest wall < Trauma, Tm. Stimulate

- Announcement of (PT) during Sampling.
- Non fasting samples

"Values of PRL"

- NL: 5-20 ng/ml
- Physiological ↑↑: < 50 ng/ml
- Drug: ↑↑ < 100 ng/ml
- Tm → 200 ng/ml (less likely if < 100).

Effects of PRL on Male reproduction:

① In physiological level: ↑ Leydig cells response to LH

② pathological level:

↓ FSH & LH. ←
- ↓ GnRH sec.
- ↓ Pituitary response of GnRH
- ↓ 5-α reductase → ↓ DHT
- Destructive effect of Macroprolactinoma on Pituit. Gonadotropic Cells.
- Direct inhibitory effect on the testes (??) ↘ Because PR Rs present in Ist late of seminef epith.
- ↓ Sexual desire → ED.

Causes of Male Hyperprolactinemia:-

① Physiological:

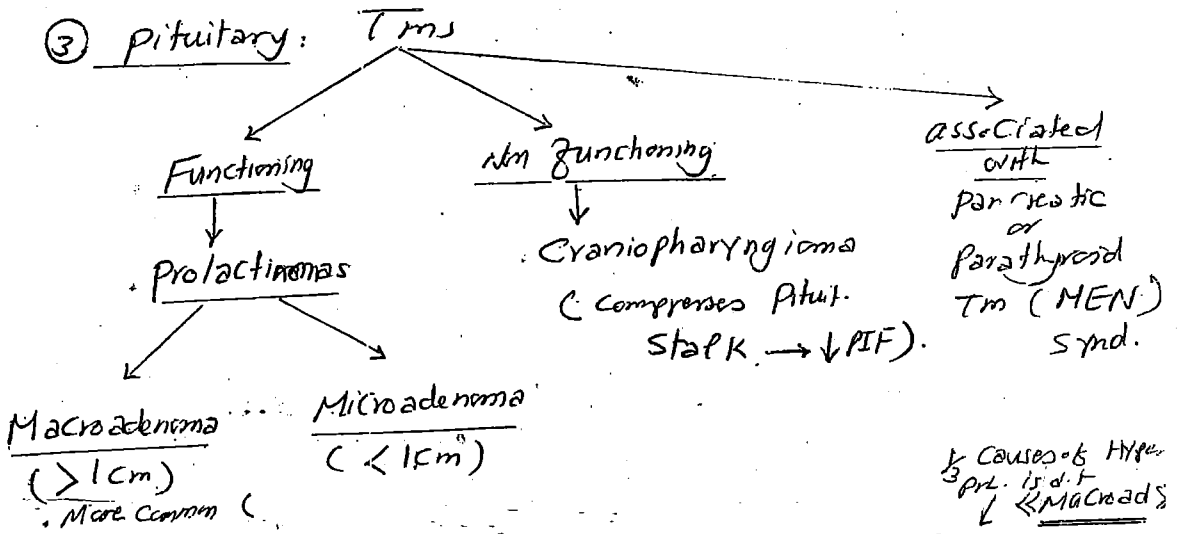
PX: Fasting Serum PRL ↑

- Exercise
- Stress
- sleep
- pregnancy (in ♀)
- Chest wall Tm or Sthm.
- Announcement during sampling
- Food.

② Hypothalamic: (d.t ↓ Dopamine sec.)

- Meningiomas.
- Vascular dis.
- Sarcoidosis.
- Histiocytosis.

③ Pituitary: Tms



· More common (↓ Causes of Hyper PRL is d.t ≪ Macroads)

· Commonest Cause of HyperPRL, is Pit. Adenoma (or)

· Usually: ↑ PRL > 200 ng/mL (level < 100 ng/ml → less likely Tm).
↓ Macro adenoma

④ Ectopic PRL Secreting Tm:

· Bronchogenic Carcinoma
· Hypernephroma.

⑤ Hepatic & Renal failure:

· ↑ PRL in d.t ↓ Clearance
· also: in LCF: ↑ Estrogen ← ++ pituitary → ↑ PRL; ↑ SHBG → ↓ Free T
· in RF: Hyperprolactinemia not corrected by renal dialysis but by Renal Transplantal (indicating: that Causative factor is in the renal parynchema).

⑥ Endocrinopathies:

· Hypothyroidism → ↓ T3, T4 → ↑ TRH → ↑ PRL.
· Hyperthyroidism → ↑ Conversion of T. to (Estr.) → ↑ PRL, ↑ FSHB
· Acromegaly [associated ↑ PRL.]

7. Drugs (PRL: Not > 100)

- Antidopaminergic → phenothiazines, Chlorpromazine, Prometha Zine (antihist.)
- Anti depressant → dibenZaZepine
- Anti HTN → Aldomet.
- Cimetidine.
- Morphine.
- Eostrogens (## of < Cancer prostate / Transexualism)

8- **Macroprolactinemia:** apparent increase in serum prolactin without symptoms. In this condition, serum prolactin molecules can polymerize and subsequently bind to immunoglobulin G (IgG). This form of prolactin is unable to bind to prolactin receptors and exhibits no systemic response. In the asymptomatic patient with hyperprolactinemia, this condition should be considered. If this condition is suspected, specific serum immunoassays must be performed to detect this form of prolactin. Women with macroprolactinemia are able to conceive. This condition generally requires no treatment.

(Hyperprolactinemia + No symptoms → ??)
d.t binding of Ig G.

Diagnostic Aspect:

- Generally Hyperprolactinemia is rare among the otherwise Normally men with infertility. So routine screening for PRL in Cases of infertility is not useful.

No Need For Isolated Mild MPRL as it doesn't affect Spermatogenesis.

- The invs. is only indicated if ↑ PRL suspected clinically: [C/P of Hyperprolactinemia]
  - Manifs of MCT (Headache & Visual field defects).
  - Gynaecomastia.
  - ↓ Libido
  - ED.
  - Retrograde ejac. (Sometimes).
  - Infertility.
- Invs: ↓ FSH, LH & T
  - Imaging → CT or better MRI (Sp. Microadenoma)
  - Bone density assesment for those ↓ T.

Craniopharyngioma & Adenoma → MRI

Treatment

I. 1st generation Drugs

(Bromocriptine = Parlodel® tab) tab < 2.5 mg / 5 mg ✓

- Mech.: Dopamine agonist → ↓ PRL
- dose: Start ē 1.25 mg ld (dt its Hypotensive effect) at night → ↑ gradually to 7.5 mg ld.

قرص = ½ قرص
½ قرص = ¼ قرص
يزاد تدريجيا
٣ أقراص

- Follow up every 3-6 ms by
  - ↓ Manifs. of ↑ICT (Headach & Visual field)
  - improved libido / ED
  - Normalizat of PRL level (< 15 ng/dl)
  - ↓ Tm size by MRI

→ Success in usually Need 1-2 Ys.

- S.E:
  - Nusea
  - dizziness
  - HypoTN
  - Nasal stuffness
  - Cold Hands
  - Constipation.

II. 2nd Generation Drugs. → ## Choice

(Cabergolin = Dostinex®)

- Mechanism: Dopamine Agonist
- dose: Tab: 0.5 mg.
- Adv: (1.) Selective.
  (2.) Potent.
  (3.) Prolonged duration of Action. ← طويلة المفعول تدريجية
  (4.) lesser S.E
  (5.) Good Compliance (Weekly dose)
  (6.) Excellent results.

dose: Start ē: 0.25 mg; ↑ grad / 4 w (based PRL level) & Continue for 6 ms after NL PRL

- NB

Pituitary adenoma

- Microadenoma → Medical Rx (لكنها بتعيش)
- Macroadenoma → Medical Rx → (3-6m)
  - Effective → Continue Rx for the Tm shrink
  - Failed → Surgical Rx (Transsphenoidal or Endoscopic removal.)

- Any infertile patient Complaining of:
  - ↑ ICT (Headache)
  - Blurring & Visual defect.
  - ↓ Libido
  - ED

↓

- Prolactin level
- MRI.

5. Hemochromatosis:

. def. AR disorder, in which there is Excessive deposition of Iron in many Tissues as:

- pituitary
- Hypothalamus
- Heart
- liver
- Pancreas
- skin

. C/P . Age: 40-60 yrs (long time needed for Fe+ deposition before S&S appear)

- Triad of:
  - infertility
  - ↓ libido
  - ED
- other features:
  - Abd. pain
  - Arthralgia
  - DM
  - HSM
  - Bronzed skin.

. Inv. ① Serum iron & Transferrin

② MRI (iron is Paramagnetic).

. Rx: → iron chelating Agents.

Peripheral Organ Causes

- Adrenal disorders
- Thyroid
- ↑ Estrogen

Adrenal Hyperfunct⁻ (↑ Cortisol)

1. Adrenal Hyperfunct⁻ :
   - Hyperplasia
   - Adenoma
   - Carcinoma
   - Cushing
2. Ectopic ACTH Tm
3. Exogenous Cortisol

↑↑ Cortisol → -ve feed back on pituitary → ↓ FSH & LH → ED d-t:

- -- % Leydig cells
- Ass. DM
- ↓ libido
- Anti HTN.

↓ So CIP

1. Cushing aid features
2. ED
3. ↓ libido
4. infertility.

Adrenal Hypofunct⁻

- Adrenal Failure : (Addison)
  - inf.
  - Infarction
  - CAH "Dr"

↓ All

↓ Cortisol → ↑ ACTH → ↑ Adrenal ↑ Androgens → -- GnRH.

↓ CIP

- Fatigue
- W.L loss
- HypoTN
- ↓ sexual funct⁻

Estrogen Excess

Causes :

- Sertoli cell Tm
- Leydig Tm
- LCF
- Excess obesity.

↓

- Estrogens :

2 Mechanisms

- ++ Pituit → ↑ PRL
- ↑ SHBG → ↓ Free T.

CAH → See Hirsutism.

Thyroid disorders

- Hypothyroidism : → 2 Mechanisms
  - ↑TRH → ↑ PRL
  - Ass. auto immune mech. at level of Both < Testes / thyroid.

- Hyperthyroidism : → 2 Mechanisms.
  - ↑SHBG → ↓ Free T.
  - ↑ Aromatization of T. to Estrogen → ??

- NB . Manifs usually of that of:
  - Infertility
  - Gynecomastic
  - ↓ libido
  - ED

- on Both disorders the patient usually presented by the dis. manifs rather than infertility.

- Hyperthyroidism & Androgen resistance Synds:

  2 conditions in ♂ ED Not ass. ♀ low Androgen level & this can be Explained by:
  - ↓ Free T : in Hyperth.
  - ↓ T. Act : in Androgen resistance Synd.

Causes of Male Infertility

- **Hypogonadism** (Testicular failure = Testicular & pretesticular Causes of infertility)
  - **Hypogonadotrophic Hypogonadism** (pretesticular = Endocrinal infertility) — 2ry testicular failure or Hypogonad.)
  - **Hypergonado-Tropic Hypogonadism.** (1ry Hypogonadism or 1ry Testicular Failure or Hypog.)
  - **Normogonado-Tropic Hypogonadism.** (IH)
- **Post testicular disorders.**
  1. deposition disorders
  2. Transport disord.
  3. Motility disorder.

Another Classification

- **Pretesticular** (2ry Hypogonadism)
  - Hypothalamic Causes
  - pituitary "
  - peripheral organs "
- **Testicular** (1ry Hypog.)
- **Post-testicular** as above.

اسئلة بدان

- **Hypogonadism** (Testicular Failure)
  - 1ry (Testicular Causes / 1ry " Failure.)
  - 2ry (Pretesticular causes) 2ry testic. failure. → Endocrinal infertility

Primary Testicular Causes of Infertility (Hypergonadotropic Hypogonadism)

Chromosomal Causes

- 8 Syndromes
  - Klinefelter
  - Y chromosome

Non Chromosomal Causes

- Varicocele
- Anorchia
- Cryptorchidism
- Germ cell aplasia (SCOS)
- Germ cell arrest
- Trauma
- Tm
- Torsion
- Inflamm. (orchitis)
- Radiotherapy
- Chemotherapy
- systemic dis.
- Idiopathic
- Others
  - Granulomas
  - Sickle cell dis.
  - Excess: Alcohol, Cigarettes, Caffeine.

. chromosomal infertility

Incid: Chromosomal Abnormalities Ch BY:

~~- Affect 0.6% of General Populat~~

- Affect 1% of pts. ē NL Semen analysis.
- Affect 10-15% of pts ē Azoo. or severe oligo

(Non obst.)

Chromosomal Abnormalities include

- Klinefelter Synd.
- XX Male (Sex reversal Synd)
- XYY Male
- Noonan Synd
- Mixed gonadal dysgenesis
- Down Synd ← Extra 21 trisomy
- Myotonic dystrophy Synd
- Y chromosome Microdeletion synd.

The Most Common Cause of chromosomal Abnormalities
1. Klinefelter
2. Yq Micro-delet
3. structure Autosomal Abnormalities
4. Others
   - XXY
   - YY
   - ...

EAU (41)

· Klinefelter Synd

- "Most common chromosomal Abnormality of ♂ infertility
- affecting 1:500-1000 male births.

- Pathophysiology. AET: Failed disjunction ∴ may be at: → extra X-chromosome
  - (nondisjunction)
    - pre-fertilizat → classic
    - post-fertilizat → Mosiac.
  - ① 1st Meiotic division (Maternal AGE > Paternal)
  - ② Following Fertilization (Mosiac form of dis.)

- Types or variants:
  - 47 XXY → Classic form (80-90%)
  - 46 XY/47 XXY → Mosiac form (10% – 20%)
  - "rare forms"
    - 48 XXYY
    - 48 XXXY
    - 49 XXXYY
    - 49 XXXXY

- NB: Severity of the dis. is ↑↑ by ↑↑ No of (X) Chromosome

C/P ① Andrological Mani → Hypogonadism.

ونتيجة ذلك لا تأخر = ٣ علامات

- delayed puberty
- sexual dysfun. "Kallman synd."
- infertility

. Testes: small (< 2 cm L, < 12 ml volume) & Firm (d.to hyalinizal & sclerosis)

: Commonest presentation is: infertility & Gynecomastia.

. Features are not apparent till puberty → delayed D.

② CNS

. Most Classic Cases has NL mental state & mentality affection by ↑ No of (X).

✓. ≃ 70% having developmental & Learning disability:

- ✓ . delayed speech
- ✓ . ↓ short term Memory
- ✓ . reading difficulties.

✓. psychological & psychosocial disorders.

③ Cardiac

- . W
- . DVT
- . Venous ulcer
- . Mitral prolapse.

④ others:

- . Osteoporosis
- . DM
- . Emphysema
- . Thyroiditis.
- . Pituit. Tm
- . Breast Tm [Cancer] (70 times > NL)
- ↓ Cortisol level (علاج بالكورتيزون)
- . Testicular Tm
- . Lymphoma.

Diagnosis

Clinical Exam.

- . Eunchoid body
- ✓ Gynecomastia
- . Small firm Testes (p. 268)
- . . . . etc.

Classic ← AZo

Mosaic ← oligo

Investigations:

A. Semen analysis:
- . most (60%) → AZO
- . Mosaic Type → ± Sperms

2 ✓ FSH & LH → ↑

✓ Testost. → ↓ or Low N.

3. Karyotyping

Bono

NB (Euro/EAU)

- in Klinefelter sperms ± obtained by
  - ejaculate of Mosaic Cases
  - Ejaculate of Young Classic Cases. ← عشان كده نبقى نشفيه بدري قبل ما يحصل إعادة للكولات → Cryopreserv.
  - TESE: recovery of sperms in 30-50%
    أقصى كذا كلام

- Klinefelter pt has ↑ incid of: (based on sperm FISH studies)
  - (a). Sex chromosome abnormality
  - (b). Autosomal aneuploidies (disomy for chromosomes 13, 18, 21)

↓

So chromosomal abnormality of fetus ± obtained by ICSI

↓

So Better

ICSI c PGD is essential

AZo من المرضى ٦٠٪ منهم +ve sperm ٢٠٪ by TESE

Tt → ICSI By TESE

↳ Replacement therapy → for induction of puberty

Karyotyping (chromosomal Karyotyping):

2 Types

- **Barr Bodies Karyotyping**
  - Rapid
  - Simple
  - but Inaccurate
- **Lymphocytes Karyotyping** ↓
  - More reliable.

Results:
- 80-90%: 47XXY (classic)
- 10-20%: 46XY/47XXY (Mosiac)

- **Testicular Biopsy:**

Classical Type
- Tubules → Hyalinization / Sclerosis / Atrophy
- Leydig cells → Atrophy with focal Hyperplasia of Mostly degenerated cells. (Adenomatous clumping ↓ Cytop. granul. & Lipid droplets. clumping: ↓ diff ↓ ST mass → not true Hyperplasia).
- Germ cells → ↓ or absent.
- Spermatogenesis → rare.

Mosiac...
- at puberty: NL sized testes & Spermatogenesis
- after it: progressive degen. & hyalinization of Tubules.

- **NB:**
  - Surprisingly: (most) patients have NL ← Erect. / Orgasm. / libido
    So Exogenous Testo. ## → limited role, & may ↓↓ underlying sperm production.
  - **Azoospermia**: present in (60%) & in 20% of them → There are 80% of spermatogenesis.

* **Other invs:** ✓
- ECHO
- Bone density.

(##)
1. For puberty & libido → TRT

Mixed Gonadal DYsgenesis: (Variant of Turner)

- 45 X /46 XY
- C/P: ① Ambiguous Genitalia.
  ② Testis on one side & Streaked gonad on the other side.

Down Syndrome (TRISOMY 21)

- Most Common chromosomal disorder & the most common genetic cause of MR.
- C/P ① Hypotonia
  ② short Neck
  ③ MR
  ④ low set ears
  ⑤ Open mouth & Protruding Tongue (Scarty)
  ⑥ Cong. Heart dis.
  ⑦ ↑ incid of Leukemia.
  ⑧ Andrologically:
    - Varying degree of Testicular dysfunction
    - ↓ Germ Cell No
    - ↑ FSH & LH.

Myotonic dystrophy Synd

- AD
- defective dystrophin gene → delayed ms. relaxation after Contraction.

C/P ① Testicular Atrophy (degenerated tubules)
② Leydig Cells → NL
③ Biopsy → Severe tubular Sclerosis.

- No effective Rx.

XX Male (Sex reversal Synd):

Sex determining gen on y chromosom.

- AEt: The XX Karyotype is d.t Cross over of the Sex determining region (SRY) of the Y chromosome (= Testis determining factor) to either the X chromosome or an autosome.

cross over of SRY gene on Y to X

- CIP: 1. short stature
  2. Gynecomastia
  3. Small firm testes → to differentiate it from Klinefelter
  4. Hypospadias
  5. NO ↑ in Incid. of MR.
  6. Sclerosis of Tubules.

By points: 1, 4, 5 (Not in Klinefelter)

LH & FSH ↑ - testosterone ↓

XYY Male (47 X YY Synd)

- incid: 0.1 - 0.4 % of New borns.
- CIP: 1. Tall stature, large teeth & pustular AV.
  2. Aggressive antisocial behavior (Criminal tendencies).
  3. Severe oligo. or Azoo.
  4. Testicular Biopsy: → Spermatogenic arrest.
  5. don't pass to the Next generations.

Criminal Tendency

Noonan Synd (Male Turner Synd). XO

- Karyotyping → XO/XY Mosaicism. 45 XO
- CIP: 1. Short Stature.
  2. Webbed Neck.
  3. low set ears.
  4. ptosis
  5. Lymphoedema
  6. CV anomalies (Left)
  7. C.L.L. Values
  8. Leydig cell dysf.
  9. Infertility.

Similar physical ch. as "Female Turner"

Y- Chromosome Microdeletion Synd.

- Intact (Y) chromosome is essential for Both:
  - reproductive system development (Gonadogenesis)
  - " " Function (spermatogenesis)

Y chromosome Has 2 arms

Short arm (Yp)

- Contain SRY gene → sex determining region of Y chrom.
- (F.) Gonadal differentiation Towards Testicular pathway → Testis
- if there is Microdeletion of short arm (SRY deletion) → "Sex Reversal" (phenotypically Female (XY))
  - Testis → No Null inhibitory substance (→ ♀ genitalia)
  - No testosterone → failure of ♂ genitalia

long arm (Yq)

(Critical for Fertility)

Has 2 parts

Heterochromatic Part (Yq12)

- Microdeletions of this part has no effect on reproduction.

Euchromatic Part (Active)

(Yq11) Sp. (Yq11.23) (interval 6).

has 4 regions (Yq11.23 interval (6)) (Loci) essential For Spermatogenesis

These Regions "Called AZFs"

- AZFa
- AZFb
- AZFc
- AZFd

→ Microdeletion → Infertility

AZoospermic Factor → Genes

Y CHROMOSOME MIRODELETIONS

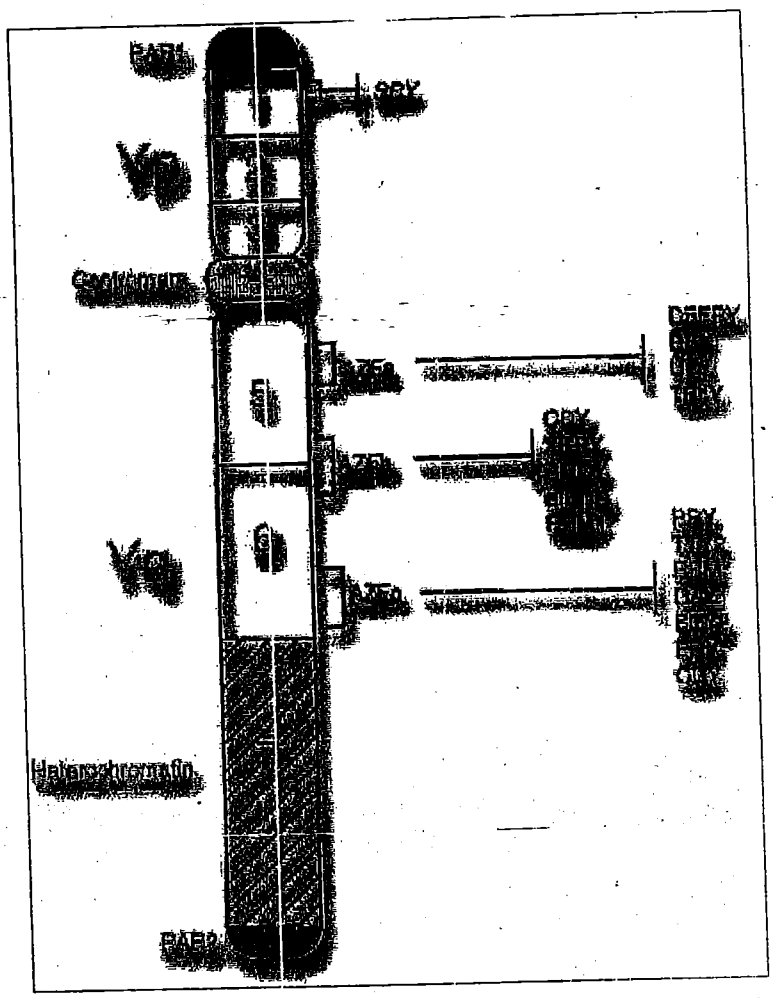


Figure 1. Schematic representation of the Y chromosome showing the seven deletion intervals. Pseudoautosomal region 1 and 2 are indicated (PAR1, PAR2).The regions AZFa, AZFb and AZFc and genes located within them are illustrated.

Microdeletions of the AZF regions have different frequency and each shown a diverse clinical phenotype (different spermatogenesi's abnormalities.). Relative prevalence of deletions in AZFa,b,c region in infertile men:

- AZFa: 5% → (Azoospermia with Complete absence of germ cells, non mosaic SCOS)
- AZFb: 10%→ (Azoospermia , SGA and SCOS)
- AZFc: 70% → (Variable phenotype ranging from mild oligospermia to azoospermia and SCOS).
- AZFa+b: 1.5%
- AZFb+c: 8.3%
- AZFa +b+c: 4%

defection of The deletions (Microdeletions) can be done BY: 1. pcr based Sequence - Tagged site Mapping
2. Southern blot.

"Not by usuall Karyotyping"

- Indication of Testing for AZF:
  - Azoo.
  - severe oligo < 5

AZF Microdeletions observed in:

- 5-10 % of Azoo.
- 2-5 % of severe oligo < 5 million.
- 0.7% of pt > 5 million.

AZF deletions Significance:

EAU

- AZFa (Rare; 5%): → SCOS (classic)
- AZFb (2nd Most Comm) → Spermatogenic (SGA) Arrest
- AZFc (Most Common: 70%): Azoo or oligo → (Mixed SCOS, late SGA)
- AZFd: OAT oligo-Azo-terato

→ TESE out-come -Ve

TESE out Come ↓ 50% +Ve

- NB: AZF a+b+c may occur

NB DAZ gene (deleted in Azoospermia gene): Cluster in AZFc & Seems to be the most important.

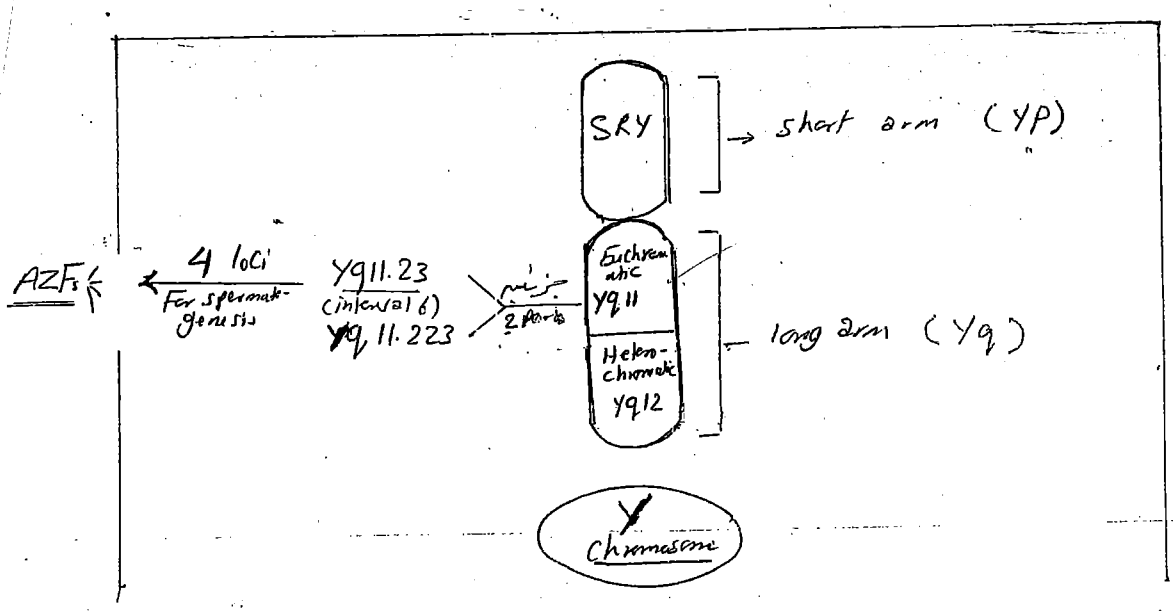


Table 9.4 Lower reference limits for semen parameters for couples with a time to pregnancy of 12 months or less

Parameter	Suggested normal value (WHO 1999)	Lower reference limit (confidence intervals) (WHO 2009)
Semen volume (ml)	≥2.0	1.5 (1.4–1.7)
Total motility (PR + NP %)		40 (38–42)
Progressive motility (a+b, PR, %)	≥50	32 (31–34)
Vitality (%)	≥50	58 (55–63)
Total sperm number (10⁶/ejaculate)	≥40	39 (33–46)
Sperm concentration (10⁶/ml)	≥20	15 (12–16)
Sperm morphology (normal, %)		4 (3–4)
Other consensus values:		
pH	≥7.2	≥7.2
Zinc (µmol/ejaculate)	≥2.4	≥2.4
Fructose (µmol/ejaculate)	≥13	≥13
Neutral α-glucosidase (mU/ejaculate)	≥20	≥20
White blood cells (10⁶/ml)	<1	<1
MAR-test (%)	<50	<50
Immunobead-test (%)	<50	<50

Germ Cell Aplasia
(Sertoli cell only Synd) (SCOS)

def. Testicular disorder ch by absence of Germ Cell (Spermatogenic cells) & so the testicular tubules only lined by Sertoli Cells.

AET 1. Idiopathic → most cases

2. Cong → d.t Failure of Migration of Germ cells From the Yolk Sac to the genadal ridge during IU development ∴ may be caused by:
   - Y chromosome Microdeletions e.g. AZFaxc (Azospermic factor Microdeletion)
   - Klinefelter Synd: has chic Biopsy appearance of SCOS & Leydig Hyperplasia

3. Acquired:
   - Radiation
   - Infection (Viral)
   - Cryptorchidism → undescended testis
   - Cytotoxic drugs.

Incid: . < 5-10% of infertility Cases
. 20-40% of these Cases are Mixed (SCOS)

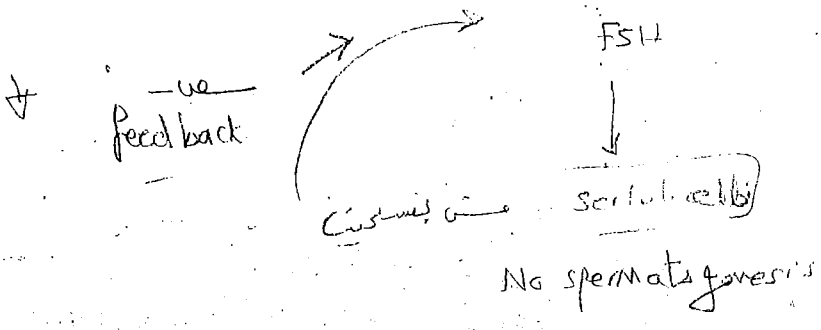
Types: 1. Complete (classical) SCOS (No Germ Cells at all) ——— (ATO)

2. Mixed SCOS (Focal) (20-40%) Variable % of tubules Contain Germ cells but Compromised.

Both in < quantity & Quality. severe Oligo

Clinical & Lab

- FSH : ↑ (2.5 - 3 folds)
- LH & T : NL
- Semen : Azoo (in complete) & oligo (in Mixed).
- Testicular V.P : (NL) — ↓↓ (but usually ↓↓)
- Karyotyping : iNL
- Test. Biopsy :
  - Absent Germ Cells. (Focal Cells ± present in Mixed Type)
  - only Sertoli Cells
  - ↓ Tubular diameter
  - NL interstitium & Leydig cells.



↑↑ → ICSI → Mixed SCOS

Germ cell arrest (Spermatogenic arrest) (SGA)

def: Histopathological finding rather than a diagnosis that indicating interruption of spermatogenic development at any level from spermatogonia to the sperm.

- arrest may occur at:
  - Spermatogonia
  - Spermatocytes
  - Spermatids

AET
1. Idiopathic.
2. Genetic (Chromosomal): AZFb & DAZ genes.
3. Acquired: Toxins, drugs, Varicocele ... etc.

- **NB** DD from Hypospermatogenesis: in which all spermatogenic stages till mature sperms are present but in a reduced No.

C/P:
1. NL testicular vol.
2. NL or ↑ FSH (but usually NL). LH, T → NL.
3. arrest of spermatogenesis ± < Partial → OAT; Complete → Azoo

- **Types**: < Partial → oligo.; Complete → Azoo.

لو فيه مشكلة في MP } AZF a → SCOS; AZF b → SGA

sperm لو فيه ← c → mild SCOS, N SGA

Anorchia

(Vanishing Testes Synd.)

- Def: Unilat or Bilat. **Absence** of Testicular tissue ē
  - NL Karyotyping (46XY)
  - DD: Atrophy (Partial or Complete) ē presence of degenerated remenants.

- Pathophysiology:

Testicular development

After 6th w
- onset of Testicular development & differentiation under (SRY) gene.
  - (of Short arm of Y Chromosome)
- [Origin: undifferentiated Gonadal systeme]

Around 8 w
- Sertoli Cell development.
- secrete (MIS) Müllerian Inhibitory Substance
- regression of ♀ genitalia.

Around 9 wks
- Leydig cell development
- Secrete Testost.
- development of Wolffian duct into portions of male genital tract.

So

- Failed development at 8 w. → Female genitalia.
- Failed " at 8-12 wks → Ambiguous genitalia. inter-sex
- Testicular loss after 14th w → NL ♂ reproductive system but Absent testis.
  - (Anorchia)

(AEH)

Congenital (Very rare 1:20000).

There are loss of Fetal testes d.t

- (2T) Trauma
- Torsion → Most Common
- Inflamm.
- (2I) Vascular Injury

unilat is 4 times > Bilat.

C/P
1. NL Karyotyping (46 XY)
2. Sexual immaturity
3. Eunuchoidism
4. ↑ FSH, LH & ↓ T
5. Regression or loss:
   at
   - 8 wk → female phenotype
   - 8-10 wk → Ambiguous Genitalia
   - after 14 wk → NL genitalia but no Testis.

Treatment

- unilat. Anorchia → No ttt
- Bilat. Anorchia with phenotypically:
  - Male
    - TRT
    - Prosthetic testicular implant into empty Scrotum (Psychologically)
  - Female → ERT → estrogen replacement Therapy

* Intersexual (Ambiguous) genitalia: → plastic surgery

Acquired

(Accidental or Medical Casteration)

- Trauma
- Torsion
- Inflamm.
- "Iatrogenic"
  - Surgical Accident during < Herniotomy / orchidopexy
  - Surgical bilat. removal in cancer dependent Testost. (Cancer prostate) — "أنوركيا Bilat Anorchia"

C/P (unilat No-prob. / em.. Bilat: →)

- Prepubertal → Eunuchoid.
- Postpubertal → Infertility + lost 2ry sex ch. & sexual dysf.

Treatment

→ TRT.

(To induce & maintain puberty & sexual funct.)

NB: to diff. bet. Anorchia & Cryptorchidism.

1. do HCG stim. test for 7 ds & asses for T. level.
   if T < ↑ → Crypto. / NOT → Anorchia.
2. U/S, CT, MRI, Exploration surgery
3. MIS level assessment.

Cryptorchidism

"إخفائي"

def: Hidden testis.

- Undescended (True Cryptorchidism)
- Ectopic (Maldescended)
- Retractile
- Atrophic

physiology of Testicular descent.

Testes are formed as a retroperitoneal organ high in the post. Abd. wall → then descend & Accompanied with its Neurovascular supply.

onset of descent:

- Before 7ms → No descent.
- At 7ms → onset of descent To the Int. Inguinal ring.
- At 9-10 ms → Complete descent (at time of birth & it is sign of Maturity).

phases of descent: (i) Transabdominal (ii) Inguinoscrotal

Factors Responsible for descent

Hormonal Factors

- Intra-abd. descent (to Ring) → (MIS) AMH
  - INSL 3 (insulin like factor 3)
- Extra-abd. descent (Inguinoscrotal) (below the Ring) → Testosterone (DHT)

Mechanical Factors

2 theories:
- Traction by...
- pressure ...

Neurological Factors

- Androgen → ++ Nuclei of genitofemoral N. → release of CGRP → Modulation of structure & Function of Gubernaculum
- "Calcitonin Gene related peptide"

Mechanical Theories

⚠ Traction Theory : d.t Traction by "Gubernaculum"

Embryologically;

→ Testis has 2 ligaments.

- Cranial Gonadal Lig.
  - Connect upper pole of Testis to diaphragm.
  - → disappear (± OHT) effect
- Caudal Gonadal Lig.
  - attached to the lower pole Testis
  - → Continous to grow & extend downward To form Gubernaculum
  - Testis → Enlarges & Swells into scrotum
  - → Traction & descent.
  - Attachment to scrotal wall

NB

- undescended Testis + Hypospadias → ?? Intersex
- Failed obliteration of processus vaginalis → Hernia or Hydrocele.

during Testicular descent; → the testis Takes a peritoneal pouch called "processus vaginalis" that's when its connection with the abd. obliterated called Tunica vaginalis. in Complete obliterated remnants of processus vaginalis called "Vestige of Processus" ⇒ may → Cong. Hydrocele or Hernia.

⚠ Pressure Theory: Testicular descent is dependent on the downward pressure on Testis by growing Abd. Viscera. (Ss Cryptorchidism, Prune belly syn, Gastroschisis.

Testicular descent

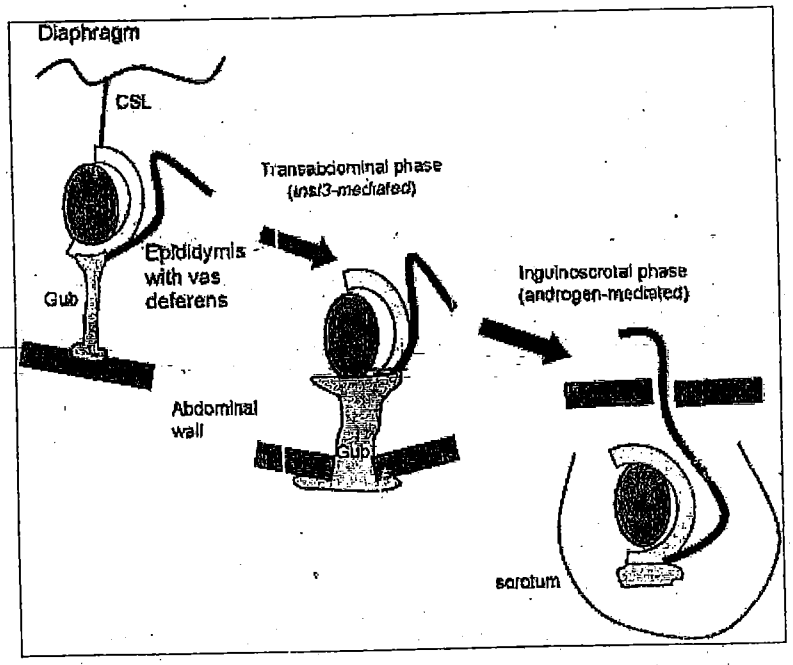


FIGURE 3-1 Stages of testicular descent. Testicular descent in scrotal mammals (such as humans and rats) can be conveniently divided into two phases. The first is the transabdominal phase in which the cranial suspensory ligament (CSL) disappears, and the testes—located near the kidneys—move into the lower abdomen. **The first phase** is under the control of the hormone, insulin-like factor 3 and MIS. **The second phase** is the inguinoscrotal phase in which the gubernaculum (Gub) develops further, and the testes move through the body wall (inguinal ring) into the developing scrotum. The second phase is under the control of androgen.

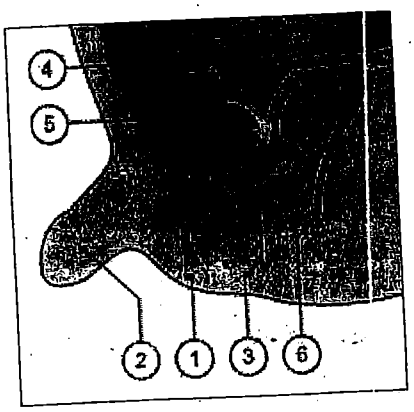
. Gubernaculum Enlargement "swelling reaction" is Controlled by:

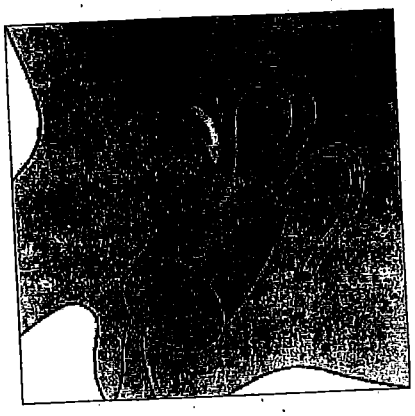
. INSL3 (recently, 2016 considered the Major Factor)
. Androgen (DHT) → (was considered " ")
. MIS / AMH
. relaxin hormone . CGRP.

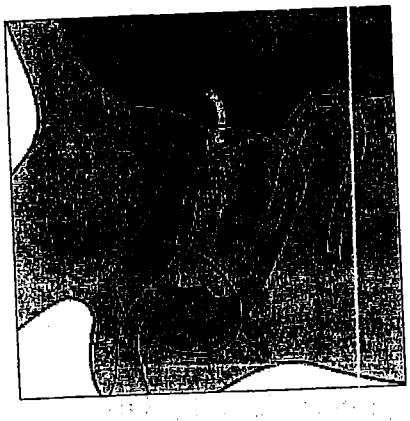
. Effect of androgen on Test. descent

. Enlargement of Gubernaculum.
. ++ Genitofemoral Nerve → ↑ CGRP → Gubernaculum Enlargement.
. ++ regression of CSL. Cranial Suspensory Ligament.

. CGRP: ↑
. Estrogens → ↓ INSL3 → ↑ Failed descent → Cryptorch.







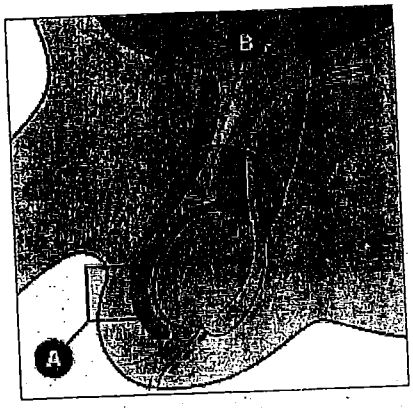


Fig. 1: The yellow arrow shows the location of the protrusion of the peritoneum and the beginning of the testicular descent into the inguinal canal.	**Fig. 2:** In this diagram, the beginning of the formation of the vaginal process is visible. It enters with the testis into the inguinal canal. Shown in blue is the gubernaculum that becomes increasingly shorter.
Fig. 3: Between the 3rd and 7th month of pregnancy the testes remain near the inguinal canal in order to pass through it. The vaginal process lengthens while the gubernaculum shortens, thereby drawing the testis, the deferent duct and its vessels on both sides downwards.	**Fig. 4:** In the 9th month of pregnancy (but also sometimes only after birth) the testes reach the scrotum. The vaginal process forms now a serous bilaminar structure on the front side of the testis.

Testicular Descent

For details: Genetics and Hormones in Testicular Descent, Int J. of endoc. And Metabolism, 2011.
Sexual Differentiation, Endotext.

. NB Cut. disorders ass. with Cryptorchidism.

. ATaxia Telangiectasia
. Rothmund - Thomson Synd.
. BCN Synd.
. Icthyosis

. **Epidemiology of Cryptorchidism:**

- affect 3% of Full term → ↓ to 1% at end of 1st Year.
- " 30% of prematures.
- 7% incid. in Sibling Boys: [Genetic Cryptorchidism]
- 80% unilat: (Rt > Left) — Rt (50%), Left (30%)

% of descent:
- during 1st Year: 75-90% (غالبا ادرك post natal Gn surge at 1-4 ms)
- after 1Y: Very rare (0.8%)

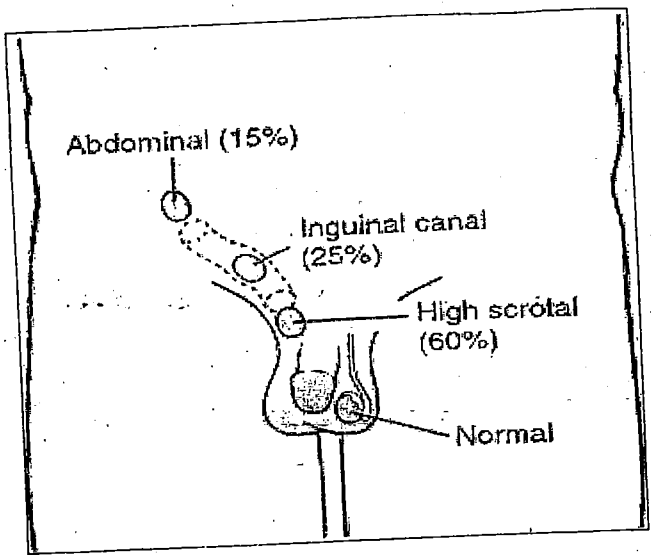
. **Predisposing Factors:**
- Mechanical Failure: peritoneal adhesion or short Vs.
- prematurity.
- LBW.
- Twins [Genetic Cryptorchidism]
- Maternal exposure to Estrogen & NSAIDs (Paracetamol, Ibuprofen) during 1st trimester.

C/P

Undescended (True Crypto.)
- arrest of descent along its NL pathway of descent.
- Site may be: High or low
  1. Intra abdominal: at & above the inguinal ring
  2. Intra canalicular: inside ing. canal
  3. Emergent: bet ext. ring & Scrotal Neck.
- (in Most cases: arrest occurs during inguino-scrotal descent)

Ectopic (Maldescended)
- migration of Testis From its NL pathway of descent to an Ectopic sites (after its Exit of the Ing. ring).
- Site may be:
  - Perineum
  - Femoral region
  - infront of S. pubis
  - Superficial inguinal pouch
  - may be d.t: abNL Gubernaculum which mis-directs the Testis to Ectopic sites.

Retractile (very marked at 5-6%. No effect on Test. Func.)
- Testis easily withdrawn From its NL Intrascrotal position to high up along the course of descent (معلق الشبح)
- AEt ± d.t: Strong Cremasteric Reflex / Wide Ext. ring
- at puberty → ↑ Permanent S position.



- Levels of Arrest of UDT

∴ Undescended has higher incid. of Complications.

- Ectopic less incid. of < infertility / Mg
- Retractile: No risk

Complications of Cryptorchidism

1. Infertility
2. Malignancy
3. Associations

(1) Infertility:

- Causes: (1) ↑ Temp:
  - Leydig → remain functioning (as in Varicocele)
  - Sertoli & 1ry Spermatocytes → degenerate early → suppress spermatogenesis
  - ABP & Sertoli cell marker → G. protein → Need 34 °C! degenerated
- (2) Endocrinal: ↓ LH
- (3) ↑ Incid. of Ass.:
  - SCOS
  - Arrest
  - Carcinoma in situ.

- Incidence of ~~infertility~~ ↑↑ By:
  1. ↑ durat~ of undescent
  2. Bilat > Unilat.
  3. Higher posit~ (Abd > Inguinal)

So Males è Bilat. testes are Normally androgenized

(2) Malignancy

[A] Incid (risk)

- 40 times higher risk > NL testis.
- 10% of testicular Tms arise on top of undescended testis.
- ✓ higher posit⁻ are more risky > lower posit⁻ (abd. testis → 4 times risky > inguinal)
- ✓ Cryptorchidism → ↑ risk of Mg of contralat. testis.
- ⚠ (Mg) → the risk of Mg remains high even if the testis brought to scrotum.

[B] onset: at or after puberty (but may affect children & infants)

[C] Type: the most common: Seminoma > Embryonal Carcinoma
if crypto + intersex → Gonadoblastoma is the most common.

[D] Etiology: A/o ↑ d.t Cryptorchidism itself but the predisposit⁻ d.t inherent in testis ?
evidence:
- Risk remains even after orchiopexy.
- Risk is higher in ↓ contralat. NL testis.

(3) Associations:

[A] Hernia:
- risk is ↑ d.t associated processus vaginalis (90%) but the neck of sac is too narrow to allow entery of abd. viscera → so clinically obvious hernia is uncommon.

[B] Torsion
- because the undescended testes is broader than its mesentry
- risk ↑ after puberty (either d.t < ↑ size or ↑ Tm)

[C] trauma

[D] Atrophy: Common ↓ complication of orchiopexy.

Diagnosis

1. Hx
2. Exam.
3. Inv.

1. History:

- determine whether it was palpable or not.
- Past HX: of inguinal surgery.
- Prenatal HX: prematurity, Maternal Hormonal ttt.
- FHX: Crypto., Hypospadias, intersex.

2. Examination:

شروط وطريقة الفحص:

1. warm place to avoid cremastric Ms contraction
2. Relaxed patient
3. Inspect for a time for:
   - other testis → Contralat. Hypertrophy
   - Scrotum: → Bifid, Hypoplastic, Pigmentat.
   - Penis < length, Hypospadias.

"NB": Hypospadias + Cryptorch. = DSD (intersex) (Disorders of sexual differentiation)

4. Choose 3 positions:
   - **Supine**: to detect < undescended, Ectopic
     - (Milking Motion) starting from the Iliac Crest down to Scrotum (ممكن نستخدم صابونة أو) OP.
       - Palpable → [illegible] ↓ intracanalicular or Emergent
       - Not Palpable → Failed palpation
   - **Squatting** (eleminate Cremasteric reflex): to detect Retractile (يشدها سوسولتي)
   - **Standing**: To detect ass. Hernias.

5. Failed palpation: may be:
   - Anorchia or
   - Intra-abdominal Testis.

How to diff ??

Inv.

HCH → ++ leydig cell → ↑ testl

① Lab

1. Semenogram : Azoo or oligo or Norma.
2. HCG stim. test : to diff. < Anorchia & non palpable (Abd.) testis. (Bilat.)
3. Hormonal inv: → MIS → ↓ in Anorchia

also MIS level > 5ng/ml ← 2.
↓
Exploral

→ Unilat → No Need.

→ If / Bilat. Unpalpable or unpalpable Unilat + Hypospadius. → Rule out (DSD) & do:

or Ambig. Genit.

- Chromosomal Analysis
- 17 hydroxy Progestrone
- LH
- FSH
- Testosterone

② Imaging Studies: (Little or No role in Cryptо.)

- US
- CT
- MRI
- Angiography

} have unacceptable False +ve & -ve Results.

- Diagnostic Laparascope : Most efficient & reliable for Identification of Intra-abd. testis.

③ Testicular Biopsy: For < Germ cell changes CIS.

- Range from NL - Acq. germ cell Hypoplasia & Leydig cell hyperplasia.
- Severity : of changes Correlated < abd. Testis / orchidopexy
- Incid. of Carcinoma in Situ:
  - in children → 0.4%
  - infertile Adult → 8%

Hernia

1. Retractile: Annual Exam ② → ① can be manipulated to scrotum → reassurance as most cases descend at puberty
   → ② don't descend at puberty or become Ascending (can't be manipulated to scrotum) → Orchiopexy ③

2. Ectopic: Orchiopexy (no effective medical ht; why??)

3. Undescended: Aim: To avoid complication
   (a) to allow for NL anatomic position of Testis & prevent of bad psychological effect of empty scrotum.
   (b) prevention of complication e.g Mg & infertility.
   (c) Correction of Associated Hernia.

Onset = when to start

- after 1st y: to allow for Spont. descent.
- Before 2nd y end: To prevent testicular damage.
- after 4 m (4-6 m): because chance of Spont. descent after 4 m is low.

Types of Ht

Medical Ht

>3 yrs

Best Results if:
1. Older Boy
2. lower level of Testis.

. success rate: ??20%

Surgical

- Orchiopexy
  - ✓ the Gold Standard for ht of UDT
  - ✓ Repair ass Hernia / Torsion
- Orchiectomy
  - ✓ Failed Orchiopexy
  - ✓ Atrophic testis
  - ✓ Adulthood case
  - ✓ DSD (Trix of M

Medical (Hormonal) ttt of undescended Testis.

HCG (pregnyl = Chorionic factor) ®

Mech. ++ Androgen sec. → descent by ?? mechanism but ± through effect on < Cord / cremasteric Ms. >.

- Dose
  - 0–2 ys → 250 IU
  - 2–5 ys → 500 "
  - 5–10 ys → 1000

  مرتين كل اسبوع لمدة ٥ اسابيع

- S.E: (1) Relapse: بعد توقف العلاج تطلع تاني
  - (2) Virilization [Precocious]:
    - ↑ scrotal rugae
    - ↑ Pigm.
    - ↑ Pubic hair & penile growth
    - dose > 15000 IU → epiphyseal closure.
- Success rate: (25 – 50 %)
- Better results if:
  - Bilat > unilat
  - Inguinal > intraabd
  - Age > 3 ys.
- Child ttt by hCG; Fertility rate will be:
  - 50–60% if unilat
  - 35–45% if Bilat.

GnRH (Nafraline or buserline) ®

200–400 Mg Nasal sprays 3 times / day For 4 ws

↓

Better results.
- (↓ 1ot / 16ms) less relapse
- less virilization

Combined ttt

Combined ttt (7 ws)

400 mugm GnRH 3 times/d for 3 ws

Then → 1500 IU / w hCG for 4 ws

HL

Orchiopexy (Emedicine Urol. Surgery 2009)

Several surgical approaches to the undescended testis have been described. The approach chosen is determined by the position of the testis and the surgeon's expertise.

The palpable testis can be approached from a scrotal, subinguinal, inguinal, or suprainguinal approach. The nonpalpable testis can be approached using an inguinal, suprainguinal, or laparoscopic approach.

Routine testicular biopsy during orchiopexy is not recommended and should be considered only in cases involving prune belly syndrome, ambiguous genitalia, abnormal karyotypes, or postpubertal adolescents or men. Some authors have recommended that, if the biopsy reveals carcinoma in situ, repeat exploration and unilateral orchiectomy should be performed. In bilateral cases, radiation therapy may be useful.

Surgical pearls regarding the palpable testis:

Look for the testis after incising the Scarpa fascia to avoid injuring a testis and its cord found outside of the external inguinal ring (ectopic testis in the superficial inguinal pouch).

Divide all attachments, including the gubernaculum, the cremasteric fibers, and the lateral spermatic fascia.

Identify the patent processus vaginalis in the anteromedial surface of the cord, separate it from the cord structures, and perform a high ligation; be careful not to trap the vas or vessels.

Place the testis in a subdartos pouch.

Surgical pearls for the nonpalpable testis:

Preference should be to carry out diagnostic laparoscopy versus inguinal exploration.

Blind-ending vas and vessels confirm the diagnosis of a vanishing testis and do not warrant further therapy. Consideration should be given to exploring the contralateral scrotum and placing some anchoring stitches to prevent possible testis torsion on the other side.

Vessels entering the internal inguinal ring require further inguinal or scrotal exploration to identify the undescended testis or testicular nubbin.

In patients with findings of a vanishing testis or a testicular nubbin, fixation of the contralateral testis fixation should be considered but is controversial.

A small intra-abdominal testis or an abnormal testis requires orchiectomy.

Maneuvers to increase length of an undescended testis

The Prentiss maneuver involves rerouting the cord under the epigastric vessels or the division of epigastric vessels.

The internal inguinal ring can be opened to perform more complete retroperitoneal mobilization.

The Fowler-Stephens principle involves dividing the testicular vessels to allow the blood supply to the vas deferens to keep the undescended testis viable. The testicular vessels should be divided away from the testis.

orchiectomy ± < one stage / 2 stage → or autotransplantation Technique (ligating the test. artery to infertility)

Testicular autotransplantation can be performed by transecting the testicular vessels and by performing a microvascular anastomosis to the inferior epigastric vessels

Success rates

Orchiopexy for palpable testis (scrotal, inguinal and suprainguinal) - 80%-90%
Orchiopexy for nonpalpable testis:
- Inguinal approach - 60%-88%
- Suprainguinal approach - Up to 95%
- One-stage Fowler-Stephens procedure - 67%-96%
- Two-stage Fowler-Stephens procedure - 77%-95%.
- Microvascular transplantation - 83%-96%
- Laparoscopic orchiopexy - 80%-95%
- Laparoscopic Fowler-Stephens procedure - Up to 96%

Complications:

* infection of the incision
* bleeding
* damage to the blood vessels and other structures in the spermatic cord, leading to eventual loss of the testicle
* failure of the testicle to remain in the scrotum (This problem can be repaired by a second operation.)
* difficulty urinating for a few days after surgery

(الخصية)

. ↑ length of testes by freeing the cord from its surrounding

. # done as:
  1. 1 stage
  . 2 stage
  . Autotransplantation

. Most common complication ?? Atrophy (d.t test. Vs injury)

. Results
  Success rate
  Fertility rate

. Palpable : 80-90%
. Non " : 60-95%

NB: Hormonal treatment for cryptorchidism :

- Orchidopexy remains the gold standard primary treatment for unilateral UDT. "Considering the poor efficacy, possible side effects of the treatment and delay of definitive treatment (with the attendant sequelae of late treatment), the general use of HCG and GnRH in cryptorchidism cannot be recommended." (Canadian Pediatric Surgical Wait Times Project: Clinical Practice Guidelines for Cryptorchidism – in press).

• Testicular Torsion (مهم جدا)

(Spermatic torsion) اسم اخر

def rotation of testis along its Axis d.t twisting of the Spermatic Cord

Epidemiology:

- Incid: 1:125 ♂
- Age: 2 peaks <
  - Neonatal or prenatal. أغلبها بعد أسبوع من الولادة
  - Childhood or Adulthood: 12 - 18 Ys (75% of torsion cases < 20 Ys)
- Morbidity: depends on (time) elapsed between Torsion & detorsion; if:
  - ✓ detorsion within 6 hrs → salvage rate 80-100
  - No detorsion for up to 24hrs → Salvage rate (Zero

Types: Torsion:

→ **Neonatal (Extravaginal)**

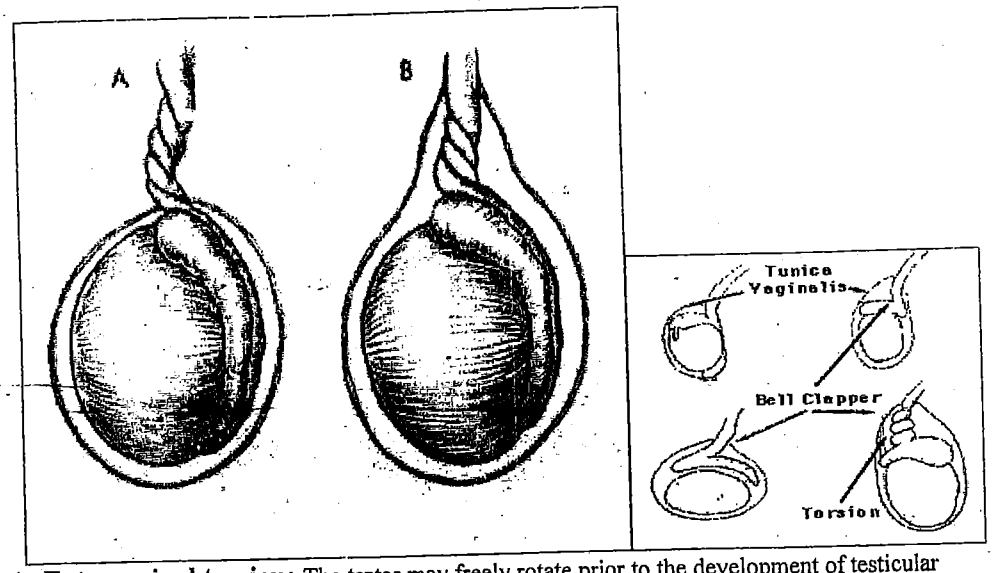
- onset <
  - prenatally → Anorchia
  - or
  - postnatally. 1st 7-10 days after birth. (البدايه)
- at this time tunica not yet Fixed to scrotal wall → Testis & Tunica are free to move inside scrotum → rotation of Both.

(Cord rotation or twisting occurs proximal to Tunica) ↓ or outside.

→ **Childhood & Adulthood (Intra vaginal)**

- in NL testicular suspension the testis & Epid. are enclosed in T. vaginalis which is attached or Fixed to scrotum after Neonatal period.
- So How does it occur?? d.t Bell clapper de

Types of testicular Torsion



A- Extravaginal torsion: The testes may freely rotate prior to the development of testicular fixation via the tunica vaginalis within the scrotum. In the neonatal age group, the testicle frequently has not yet descended into the scrotum, where it becomes attached within the tunica vaginalis. This mobility of the testicle predisposes it to torsion (extravaginal testicular torsion). Inadequate fusion of the testicle to the scrotal wall typically occurs within the first 7-10 days of life.

B- Intravaginal torsion: In patients who have an inappropriately high attachment of the tunica vaginalis, the testicle can rotate freely on the spermatic cord within the tunica vaginalis (intravaginal testicular torsion). This congenital anomaly, called the ***bell clapper deformity***, can result in the long axis of the testicle being oriented transversely rather than cephalocaudal. This congenital abnormality is present in approximately 12% of males, 40% of whom have the abnormality in the contralateral testicle as well.1 The bell clapper deformity allows the testicle to twist spontaneously on the spermatic cord.

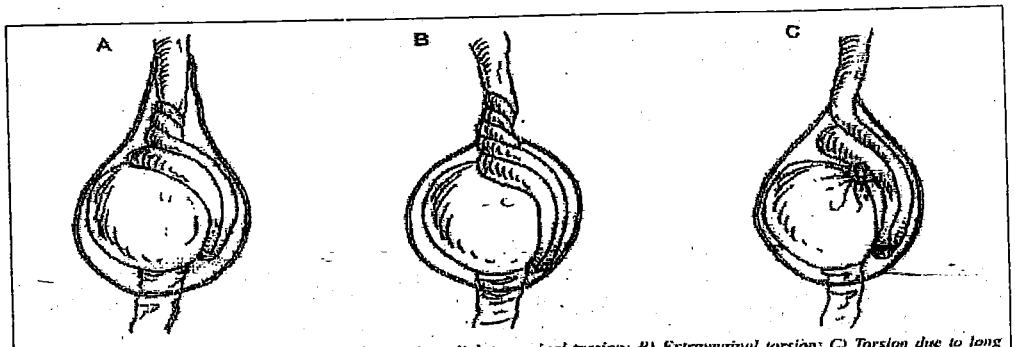


Figure 1 – Classification of types of testicular torsion. A) Intravaginal torsion; B) Extravaginal torsion; C) Torsion due to long mesorchium.

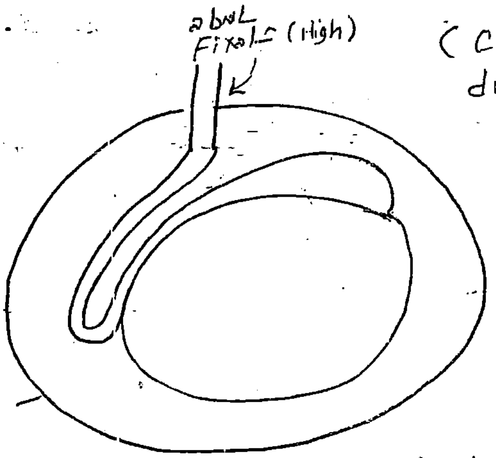
C- Long mesorchium: A large mesentery between the epididymis and the testis can also predispose itself to torsion, although this is rare

Ball Clapper deformity Ch BY

- Tunica Completely surrounds the testis ē Absence of NL post. testicular Anchoring To tunica so testis → Float, freely mobile, with longitudinal lie inside Tunic → Intravaginal torsion.
  (Attached highly to the Cord).
  (Cord Twisting occurs distal to or inside Tunica).

So Expl. ... multiple

1. lack of fixation of tunica to post. surface of Testis & Epid & its fixation high up to cord.
2. Horizontal lie of testis & Floating



- Horizontal lie & Floating
- Tunica attached high up at the Cord.

Pathological Effects of Torsion:

Effects on

Ipsilat. testis (affected testis)

↓

Testicular Artery occlusion

↓

- **2 hrs** → 1ry Spermatocytes Show Cytoplasmic changes
- **after that** → Germ & Sertoli Cells
- **after 6 hrs** → Severe damage of all Cells & Phagocytosis.

Contralat. testis (Healthy testis)

↓

Sympathetic orchiopathy

- affected testis → disturbed Blood Testicular barrier → release of sperm Ags. in Circulation → Antisperm Antibs → attack of other testis.

* C/P:

- Predisposing Factors < Cryptorchidism / bell Clapper deformity
- onset: either Spontaneous or following < Trauma / Exercise / ~~Coitus~~ Exertion

→ [A] Manifs: Severe unilat. testicular pain ass= ē lower abd. Pain, vomiting & Nusea.

NB

Blue dot sign:

. Torsion of Appendix testis ∞ leads to formation of Small Tender bluish nodule at upper pole of Testis that can be seen through the scrotal skin.

[B] Exam:-

- Scrotum → Erythematous, Edematous & Tender
- Cord: → thickened ē Absence of Cremasteric reflex.
- Testis → elevated ē abnormal axis & position.
- Blue dot sign ??

- DD: (1) Epididymo-orchitis
(2) Strangulated Hernia.
(3) Hematocele
(4) Hge inside tm.

	Epididymorchitis	Torsion
onset	. gradual	. Sudden
Fever	. ±	. -ve
. Nusea & vomiting	. -ve	. +ve.
Scrotal Elevat= → . Prehn sign	. +ve (relief pain)	. -ve (no relief)
. Doppler	. ↑ or NL testicular perfusion	. ↓ perfusion
. CRP & ESR	. ≥ 24 mg/ml & ≥ 15.5 mm/H	. NL.
Age:	↑s/. → usually adult	↑s/. → < 20y

NB

- Acute Scrotal Swelling in Children —لازم تفكر→ Torsion until proved other wise.
- 2/3 of patients → Hx & Exam are diagnostic.

Invs:

CDU
- ↓ testicular perfusion
- ± Nonconclusive in some cases.

Radio Isotopic Scanning

Surgical Exploration
↓
the single most important diagnostic & therapeutic procedure
علشان لو انتظرت لحد ما يعمل الدوبلر حتكون
(lost testis)
↓
The Golden rule is:
occasional Explorations without torsion are Expected & are far better than delayed or missed Exploration in pt. c̄ Torsion.

لازم [illegible]

Surgical Exploration
↓
detorsion (untwisting) of the cord
+
wrapping of testis c̄ warm saline sponge
then
((إصطالين))

- Color of testis → red
- Hge from tunica "albuginea"
↓
Viable testis
↓
Orchiopexy

- Color of testis → remains cyanotic
- No Hge from tunica
↓
dead testis
- Ipsilat. orchiectomy
- Contralat. → orchiopexy.

Testicular Tms
(Mg Tms of Testis)

- **Germ Cell Tms. (GCTm)** (95%)
  - Germ cell CIS
  - **Seminoma** (40%) (Commonest testicular Tm)
    - Classical
    - Anaplastic
    - Spermatocytic
  - **Non Seminoma** (Seminoma + other cell lines) (2nd most Common testicular Tm.)
    - Teratoma
    - Choriocarcinoma
    - Embryonal
    - Yolk Sac Tm.
- **Non Germ Cell Tm.** (NGCT) (5%)
  - Leydig Cell Tm
  - Sertoli Cell Tm

NB
- Seminoma: arise from Germinal Epith. of SNT.
- Non Seminoma: From Embryonal Stem Cells

Epidemiology of Testicular Tms:

1. **Frequency:**
   - USA: 9000 Case/Y.
   - Highest incid. in: المانيا / نيوزيلاندا / الدول الاسكندنافية
   - lowest incid.: USA / Asia / Africa.

2. **Race:** whites > African (5:1).

3. **Age:** Peak 15 – 35 Ys. or (20–40)
   - NB:
     - Seminoma: Classic 25–45 Ys. / Spermatocytic: 60 Ys.
     - non: 15 – 35 Ys.

4 Risky patients:

(I)
- Infertility.
- Intersex.

(C)
- Cryptorchidism.
- Contralat GCTs.

- Atrophic testes.
- Mumps
- Maternal Estrogen Exposure.

- Past H. & FH.
- Cong. Anomalies of < Penis, Kidney, testicles.

• Clinical presentation of Testicular Ca:

- Most Cases → painless testicular Mass
- Few Cases (20-40%) → Pain, Swelling & Hardness.

Other presentations:

1. Recurrent testicular ~~Bleeding~~ & Hematoma
2. Epididymitis/~~Epididymorchitis~~.
3. Torsion.
4. Infarct^
5. Gynecomastia (HCG secreting Tm a. ~~Choriocarcinoma~~).
6. Manifs of distant Metastases:
   - back pain
   - Pulm. Symptoms
   - CNS & Bone Metastases

NB : Specific Ch. for each Types

(1) Classical Seminoma :

- at 25-45
- Unilat
- L.N in 25% → Aortic

(2) Spermatocytic Seminoma :

- at 60 yr.
- Bilat.
- No CIS.
- No Metastases. good prognosis

(3) Embryonal Carcinoma : Common ← Rapid ↑↑ pain Metast.

- pain (15) common
- Rapid bulky growth
- Common Metastases (Lymphatic & blood)

"60's at Time of presentation" →

(4) Choriocarcinoma :

- Aggressive Type :)
- may disseminate Hematogenously → brain
- Secrete HCG → Gynecomastia.

(5) Teratoma :

- least aggressive Type.

(6) Yolk Sac Tm → usually present as large Ing Tm.

Diagnosis of GCTs

1. History
2. Exam
3. Investigations:
   1. Tm markers ✓
   2. Imaging ✓
   3. Histopathology
   4. Staging

(1) Tm Markers: ← HCG, ~~Afetoprotein~~, LDH

best

[A] Seminoma: 10% ↑ B-HCG

[B] NS
- 2. Choriocarcinoma: 100% ↑ B-HCG
- 3. Yolk sac Tm: 100% ↑ AFP
- 4. Teratoma & Embryonal Carcinoma: (No) ↑↑ < B HCG or AFP

(2) Imaging Studies:

[1.] US:
- ① detect testicular masses.
- ② differentiate bet. Testicular & Non-testicular Masses
  - Seminoma → Hypoechoeic
  - NS GCTs → Hyperechoeic.
- ③ to detect lymphatic spread into retroperitoneal L.N.

indications:
1. Test. mass
2. acute pain sp. an. ē Hydrocele
3. Non specific pain or swelling

[2.] CT on < Chest, Abd., pelvis.

[3.] CXR.

[4] CT & MRI of brain. For all ē stage III & IV & those ē ↑↑↑ marker level

(3) Histopathology

(4) Staging of the Tm:

- Stage I: limited to ← Testis, Epididymus or Cord
- Stage II: limited to retroperitoneal L.N:
  - IIA → L-N < 2 Cm in diameter
  - IIB → 2–5 Cm " "
  - IIC → > 5 Cm " "
- Stage III: Supradiaphragmatic Nodal (+) Visceral Sites.

Leydig Cell Tm

- Usually: Benign (1o/c only Mg)
- Hormonally active → Feminization or Virilization

Feminization d.t
- ↑ T. Conversion to Estrogen.
- Aromatase Activity of some Tms.

Virilization d.t ↑ T. secretion ← (so consider it in boys = precocious puberty).

NB. Leydig Tm of
- Cause Virilization
- usually Mg.

Sertoli Cell Tumors:

- May occur in association with 2 distinct multiple Neoplasm Syndromes:

① Carney Complex (MYXoma Synd):

- ⓐ. MYXomas < atrial, Cutaneous, mammary
- ⓑ. blue Nevi
- ⓒ. Endocrine disorders ← (Cushing & pituit. Tms)
- ⓓ. Testicular Tms (< Sertoli, Leydig)

include 3 Synd:

1. LAMB
   - Lentigenes
   - atrial MYXom
   - Muco Cut. MYXoma
   - Blue Nevi
2. NAME
   - Nevi
   - Atrial MYX
   - MYXoid NF
   - Ephelides.
3. Carney Complex

② Peutz Jegher Synd:

- ⓐ. Cut manifs:
  - Pigmented Spots: Perioral, Intraoral, Eyes, Hands & Feet, genital area & anus.
- ⓑ. GIT manifs:
  - Small intestine → . Intestinal polyps (< Abd. pain, Bleeding, Mg).
  - " Intussusception.

Types of Sertoli Cell Tumors:

- Large cell calcifying
- Sclerosing
- Sertoli cell Tm not other wise Specified (NOS).

Mechanism of Infertility d.t Neoplasm

Cancer associated Conditions

① Cryptorchidism:
2.8% ass. i CIS

② Genetic evidence of chromosomal anomalies in Cancer pts.

4-5 times more than normal testis.

10% of testicular tumors occur on top of cryptorchidism

Infertility 2ry To the Cancer itself:

① Destructive effect
of Tm → Severe impairment of Spermatogenesis (Hypo ↓)

② Immunological effect:
Tm → disturbed Blood Testis barrier → Anti-Sperm antibodies

③ Endocrinal Effect:
in Leydig & Sertoli Tmo → Estrogen level → infertility.

④ Psychological & physical stress → infertility

⑤ Obstructive effect
Epididymal obst.
(by) Neoplasm.

Infertility 2ry to Cancer therapy

① RPLND → Sympathetic denervation
Failed emission RGE
lack of Antegrad ejaculation (functional obstruction)

② Radiation & chemotherapy
Caused Azoo or Severe oligo (usually 2-3 months after ttt)
• dose & dur dep

So Must do Cryopreservation before therapy

- destructive
- obstructive
- Immunological
- Endocrinological
- Psychological

Varicocele

سؤال كرى

- def: dilatation, Elongation, Thickening & Tortousity of scrotal portion of Pampiniform plexus of veins 2ry to ↑↑ Pressure in the Int. Spermatic vein d.t back flow of blood in it.

- **Predisposing Factors** Why Testicular veins in Particular are More Liable to Varicose Veins ??

1. long Free Course along retroperitoneal space.
2. Lack of supporting muscles.
3. Absent or incompetent Valves.

Why left Sided Varicocele is more Common than Right Sided Varicocele ??

1. Left testicular vein is 8-10 cm longer > R.t → ↑ pressure in Left. (↑ length ⇒ ↑ pressure)
2. low No of Valves on left Side Veins.
3. Drainage of: Left test. vein at Rt angle into L.t Renal Vein; R.t Test. vein: at acute angle into IVC.
4. Nut Cracker phenomenon: Compression of Left renal Vein by: Aorta posteriorly, Sup. M.A. Anteriorly
5. dilatation of proximal Left renal vein → distal obst.

- **Right Sided Varicocele**

1. occlusion of IVC or Iliofemoral → Thrombosis
2. Situs Inversus.
3. Retroperitoneal Mass
4. "Aberrant Insertion" R.t Spermatic V. enter the Rt Renal V.

Aetiology (Types) of Varicocele:

1. Primary → Idiopathic (Common)
2. Secondary → less common & ± d.t
   - IVC Thrombosis
   - Retroperitoneal Mass ← Nephroma, Lymphoma, Sarcoma
   - Nutcracker

Incidence of Varicocele:

- Varicocele affect:
  - 20% of general population
  - 40% of Men ē 1ry infertility
  - 80% of Men ē 2ry infertility.
- Varicocele side:
  - 80% → left
  - 20% → Bilat.
  - Rare → Rt →

80% of Men ē clinically detectable left Varicocele Having Bilat. Varicocele detected by Doppler.

∴ this the Commonest Cause of ↓ semen quality in General population.

Effect of Varicocele on the testis (Mechanisms by which Varicocele Cause infertility)

Still unknown → Many theories:

1. Genetic theory: → theory of inherited genetic defect.
2. Metabolic ": → Stagnation → Toxic Metabolites Accumulat
3. Heat Theory: → See effect of Heat on Testis.
4. Epididymal ":
5. Obstructive ":

- d.t stasis: → Hypoxia → ROS; Hyperc-apnea → NO
- d.t reflux from Left renal or Adrenal veins. (Na, K, PG, Serotonin, Urea).

Varicocele → Epid. Ischemia / Epid. occlot / obst.

Varicocele → VD → Compression of Seminiferous Tubules at rete testis → intratesticular Mechanical Obst.

⑥ Immunological theory: Varicocele → disturbed Blood-Testicular barrier → Antisperm Abs. d.t passage of sperm proteins to circulation.

↑ FSH
↓ testesterone
⑦ Endocrinological theory: Varicocele → HPA dysf. (hypothalamic pituitary axis) → recycling cell dysf. } due to unknown mechanism

Diagnosis

- Clinical (3): Present-ation, Exam., Grading
- Imaging (3): CDFDU (Color Flow Doppler US), Veno-graphy, others
- Lab (3): Semen Evaluation, Endo-Crinal evaluation, Testicular Biopsy

Clinical Diagnosis

① Presentation

- usually Asymptomatic (most Common)
- Pain: dull aching pain or Heaviness
- Infertility
- Testicular Atrophy.

② Examination

1. Warm temp. if Cold → Cremasteric ms. Contract → Test-elevat → difficult Exam.
2. Relaxed patient. → Stress
3. 1st: Standing position
4. baring From umbilicus to Mid thigh:

Then

- Inspect
- Palpate

Inspection

- **Scrotum**: Thin, left side hanging lower than the Right. (بتوع هاني)
- **Varicocele** (G III) → elongated dilated ... criteria ... III Varicocele

Palpation

By hold neck of scrotum.

- **Testes**
  1. Soft, small → pathological changes of varicocele.
  2. Testicular vol. directly proportionate with spermatogenesis.
  3. Unilat. varicocele → Asymm. in size.
- **For Varicocele**
  - Can be felt as "a bag of worms" (= G II or G III)
  - ↓ if not palpable do: "Valsalva Maneuver" to detect (Grade I) ← تنح ... النفس بقوة داخل البطن → "Bearing down"
  - Impedes the VR → varicocele ± more prominent & impulse may be felt.
  - (This maneuver is done while doing gentle traction on the cord to prevent cremastric reflex)

Clinical diagnosis of Varicocele:

Has:
- 23% False -ve
- 24% False +ve

3. Grading of Varicocele (Clinical Grading)

Subclinical varicocele ← diagnosed radiologically not clinically.

- Grade I (small V): palpable only during Valsalva
- Grade II (Med. V): " without Valsalva
- Grade III (large V): " and visible through scrotal skin.

⇒ Then after Exam. in standing position & grading of varicocele → ask the pt. to take the supine position & inspect & palpate for **Evacuation of Varicocele**

- **Evacuated** (1ry or Idiopathic V.)
- **Not evacuated** (2ry Varicocele) → هاتفرغايه ؟؟ → IVC obst. or Tumour

NB: difficult papation may occur in:

- subclinical varicocele
- obesity ⇒ pendulous abdomen or scrotum
- previous surgery (varicocelectomy).
- Hydrocele
- High position of Testis inside scrotum.

oralQ. Significance of Grading: is Controversial

- Some authors stated that the size of varicocele has no relation to fertility & the small " can cause infertility like large varicocele; other authors stated that the larger the varicocele the poorer of the semen quality.

oralQ. Subclinical varicocele: varicocele not detected clinically but by imaging (what is significance)

↓

Controversial some authors stated that the repair of R.t subclinical varicocele may be beneficial only if it is ass. with large left varicocele.

oralQ. Consider retroperitoneal pathology (Nephroma) if: (Warning signs of Varicocele)

1. Sudden onset varicocele
2. Varicocele non reducible on supine position
3. Single Right varicocele.

Imaging

Color Flow Doppler U/S (CDU)

- Reliable & Accuracy rate (90%)
- Indications:
  1. inconclusive clinical data
  2. difficult palpation
  3. if There is a left Varicocele: CDU is indicated to detect subclinical & Varicocele.

Venography

(Retrograde Venography of spermatic veins).

- Most sensitive Method & Gold Standard However may have False +ve results.
- Indications: patient & Recurrent Varicocele after operation & should be accompanied with Transcatheter Embolization of Spermatic Veins at the Same Time.

Others

1. Doppler Exam
2. Radionucleotide Imaging
3. Scrotal Thermography

Criteria for Diagnosis by CDU (Not yet established).

either

- Maximum Vein diameter (or)
  - Mild 2.5-3.5
  - Mod: 3.5-4.5
  - Severe: 4.5-5.5
  - ≥ 3mm at rest. That ↑↑ & Valsalva maneuver.
  - كل نقطة تأخذ (Score 0-3) & if Total Score ≥ 9 → Diagnosis of Varicocele.
- Scoring System For 4 Points:
  1. Maximal Vein diameter
  2. presence of Venous reflux
  3. ! Sum of diameter of Veins in the plexus.
  4. Change of Flow with Valsalva.

Lab. D

Semen Evaluation

- Conventional Semen analysis
- Advanced Semen analysis
- Culture

إحتمالات شكل تحليل ع حالات
Varicocele. it may be: → (spectrum from: NL - Azoo)

1. NL.
2. Astheno.
3. Oligo. → Count usually improved ± < motility / Morphology
4. Terato. ← Immature, Amorphous; Tapering Head (صغيرة)
5. OAT (stress pattern) → in Most patient
6. Azoo. (5%)

* Advanced Analysis:
  1. AbnL HosTest
  2. AbnL ZFHEPT (SPA)
  3. " HZA
* Culture: There is high incid. of MAGI (Male Accessory genital Tract inf.) specially "Urea plasma Urealyticum"

Endocrinal evaluat.

- FSH ↑
- Testost. ↓
- GnRH stim. test
- hCG " "
- Kallikrein Test.

Histopathology (Test. Biopsy)

There may be:

1. NL Pathology
2. Hypospermatogenesis
3. Spermatogenic arrest
4. Premature sloughing of Germ Cells
5. Tubules → Hypoplasia
6. Sertoli → dysfunct. ē AbnL Sertoli / Germ Cell Junction → Premature sloughing of Germ Cells
7. Leydig: Hyperplastic

Endocrinal evaluation of Varicocele.

(1) FSH: ↑ FSH → indicate Germinal epith. damage → poor prognosis.

(2) Testost: may be ↓ & may affect the sexual functions. due to Leydig cell dysfunction

(3) GnRH stim test: in some Patients:

GnRH administration

- Before operation → Exaggerated response. (FSH & LH ↑)
- But after operation → NL Response: = good prognosis

So Can be used as a Prognostic Test to predict patients who will benefit from Varicocelectomy.

(4) hCG stim. test: some pts. ē Varicocele will have Blunted response of T. That will Normalized after operation. (↑ T but in less expected manner)

(5) Kallikrein test (Prognostic test after Varicocelectomy):

Inflammatory Mediator

- improved Semen parameters → indicate early Varicocele orchopathy → Improvement with Operation
- deteriorated Parameters → indicate: Genital inflamm. → ✗ No Improvement with Operation.
- Indifferent Results → indicate: Late Varicocele orchipathy / Other pathological Conditions → ± No improvement with operation.

Varicocele + NL Conventional semen analysis ??

↓

نعمل جراحة ولا لأ ؟؟

at First do: sperm fun: test.

Advanced analysis (e.g. SPA)

- AbNL → Operation.
- NL → No operation (Consider another Cause of infertility)

NB ≃ 15–30% of Patients c̄ NL Conventional Analysis have AbNL (SPA).

So: Varicocele + NL Conventional analysis → SPA

Causes of Stress pattern:

1. Varicocele
2. Viral inf.
3. Antispermatogenic agents (Cytotoxics)
4. irradiation or Heat Exposure.

Varicocele & Smoking: → Higher incid. of oligo > Those with either < Varicocele or smoking alone.

Varicocele + Severe oligo (< 5 million / ml)

قبل العملية لازم نعمل Cryopreservation

علشان: avoid Azo.

Unilat varicocele → Bilat effect on Both testes.

Treatment of Varicocele

Medical tt

Varicocele is an anatomic Abnormality that Can impair Sperm production & Function.

- ✓ No effective Medical tt
- ✓ Some authors: use antioxidants to ↓ ROS (still experimental)
  bl. flavos كسير Daflon

Surgical tt

Varicocelectomy

1. Indications
2. Types
3. postoperative details
4. Complications

Indications of Varicocelectomy

Adult (Married) ♂

٣ حاجات

Pain
بشرط
Severe pain
→ responding to Symptomatic tt & interfere
→ ē pt. physical Activity.

Infertility
بشروط
"USA Urological Society"
1. palpable Clinically detected Varicocele ē disturbed semen Parameters. [male]
2. wife ē NL fertility potentially Corrected Infertility.

Prevention of Atrophy
(vol < 20 ml & L < 4 cm).

Adolescent (Boys) (unmarried)

الأهم برة

1. Pain (as mentioned)
2. Significant testicular Asymmetry (> 20%) — To avoid Atrophy
3. Failure of Testicular growth detected by serial Examination.
4. Inadequate semen Parameters.
5. Very large varicocele (ē absent Atrophy or AbnL semen) → relative indication.
   تاعبه نفسيا

2 NB (ولد)

On Adult indications

Adult + Palpable Varicocele + Not attempting to Conceive (now)

↓

"أعلى إطلاق"

(To avoid Testicular Atrophy in future)

On Adolescent Boys

if young (Boys) + Varicocele without (Pain, ↓ Vol, Abnl Semen)

↓

يتم كل مرة:

1. Testicular size
2. Semen analysis.

↓

Any disturbance

↓

"أعلى إطلاق"

Good prognostic Indicators For Postoperative Pregnancies:

(ولد)

1. Varicocele if < unilat. / large
2. Testicular Vol. if average
3. Semen if < Count > 1a million normal / Motility: NL disturbed
4. Endocrinal tests:
   - NL FSH
   - GnRH test (+ve)
   - hCG test (+ve)
   - Kalli Krein test. →

< exaggerated response

Blunted response

3 indications.
- Pain
- Abnl Semen
- Atrophy.

Types (Methods) of Varicocelectomy

- Open Surgical repair
- Microsurgery
- laparoscopic
- Per Cut. occlusion.

4 approaches

1. Scrotal.
2. Subinguinal
3. Inguinal
4. Abd.

- Any procedure used as outpatient setting using any anaesth. (General, Regional or local)

Explanation

① Scrotal Approach: avoided as it ← Time Consuming, Testicular damage, Incomplete ligation

② Subinguinal & Inguinal approaches:

Most Common approaches.

Adv ① Familiar anatomy
② lower Morbidity
③ High efficacy

+ Subinguinal
→ easy Cord isolation
→ good in obese pts
→ " " these pts previous ing. surgery.

Incision:

Sub inguinal Method
incision at or Near the Pubic tubercle.

Inguinal Method
ASIS & Sp
opening the canal down to the ext. Ring

↓

- Cord isolation
- Testicular artery preservation
- Vein ligations:

In inguinal Approach → low No. of Vein ligated

Subinguinal → Higher No. Need ligat

③ Supra inguinal = Abd. approach (Laparoscopic)

"Retroperitoneal"

* Adv.
greater proximal control of spermatic vein Near its insertion at renal Vein.

* disadv.:
① High recurrence rate (15%)
d.t: ....
② Hydrocele: d.t en bloc ligation Artery & Vein.
③ Test. Atrophy.

Incision: Just medial to ASIS at level of deep ring

↓

en bloc ligation of Inf. Spermatic Vein.

test (Arabic) vein at (Arabic)

Int. spermatic a (vasal & cremasteric will compensate) to pampiniform plexus of vein → recurrance

↓

Modified Paloma operation.

↓

preserve the spermatic artery. (To avoid atrophy)

Using:
- Magnifying Mic. ①
- Doppler ②
- Papaverine injection ③

disadv. of Paloma:
(1) Recurrence
(2) Hydrocele
(3) Failed preservat. of Lymphatics

- Why Recurrence is High ??
  ① inguinal & retroperitoneal Collaterals
  ② preservation of Spermatic a. (Failed ligation of fine periarterial veins).
  ③ dilatat. of ext. spermatic vein occur in 50% → persistent varicocele after operat. → so doing. or sub ing.

Q. How to ↓↓ risk of arterial ligation. ??

- **Microsurgical Approach:**

Microsurgical Technique may be combined (best Method) with ing. & subing approaches →
① allowing optimal visualizat.
② " Identification of small anastmosing veins & Lymphatics (↓ Hydrocele).
③ Testicular a. preservation

- ↓ Test. Atrophy
- ↓ Hydrocele
- ↓ recurrence

- **Laparascopic approach:**

May be combined with Paloma Method".

- Was designed to get fast postoperative recovery
- has disadv. & Complications as compared to safe & simple open surgery.
  - ✓ Need GA
  - ✓ Risk of int. vascular injury
  - ✓ No. adv. > ing. in post op. Recovery.

• PerCutaneous Embolization:

. Access of Int. Spermatic vein Via Cannulation of Femoral Vein → Then balloon / or Coil occlusion.

. Adv: least invasive

. disadv: ① Trouble some access to vein

② postop. Complications:
. Contrast allergies
. arterial injury
. Thrombophlebitis
. Coil Migration.

Postoperative Measures

① Patient Instructions:

Inter. caus.

• Varicocelectomy done as an out patient setting (day surgery unit) → (بسترط شغل غير مجهد)

• Analgesics

• sterenous activity can be resumed after 2 w.

• avoid sexual intercourse ~ (1 w)

② Postop. discomfort:

- hardness around & beneath incision → resolve in (3w).
- Redness & Tenderness around & beneath → " few da
- Sore throat, Nusea, Headache, Constipation, General ache → may occur d.t surgical procedure & Anasth. → resolve 24 hr

(3) postoperative Complications: (أهم)

(a.) Hydrocele:
- incid: 2-5%
- d.t: Lymphatic injury
- High incid. ← Paloma operat°
- To avoid → Microsurgical Technique.

(b.) Recurrent:
- incid: ≃ (10%)
- High incid: Paloma operat° (15%) ??

(c.) Testicular atrophy:
- d.t Testicular a. injury — (10%) ← Microsurgery / Higher incid. ← Microsurgery
- Not all cases of injury will be followed by atrophy (d.t compensat° by Cremasteric & Vasal a.) (≃5% only)

(4) Post operative follow up (Semen analysis) (أهم)

أول تحليل نعمله بعد العملية بكرة بعد فترة

(5) Post operative Hf: (Empirical Hf):

HCG
HMG

↑ Improvement of semen quality & pregnancy rate

in Ph & Count ✗ 1 million

* HCG is mainly (LH) like and has some (FSH) action
but HMG is mainly (FSH) like & has some (LH) action

- Pregnyl: 1000-3000 IU, 2 times/W
- Metrodin (High Purity FSH): 75 IU, 2 times/W.

Post testicular Causes of Infertility

↓

disorders of

- **Sperm Transport** (Obstructive infertility ± AZoo)
  - **Organic obst**
    - unilat or Bilat
    - Partial or Complete.
  - **Functional obst.**
    - **Sympathetic Injury**
      - There is no ciliary Movement as in Diabetic ptn. ∴ Neuropathy
- **Sperm motility**
  - Asthenospermia
  - Globozoospermia
  - Immunologic infert.
  - Infections
- **Sperm deposit**
  - (Coital or Mechanical infert.)
    - **Intromission disorders**
      - Anatomical defermities
        - penile: deviate, Hyposp., Episp., Phimosis
      - ED
    - **Ejaculatory disorders** (see below)
      - PE
      - Anejac.

Obstructive infertility (organic obst.)

- obstruction may be:
  - unilat or partial → oligozoosp ✓
  - Bilat. complete → AZoospermia ✓
- Site of obst:
  - Intratesticular
  - Extratesticular

Obstructive infertility ch/ By
- NL FSH
- NL Test. Vol
- NL Biopsy

2)

Obstruction I:

Intra Testicular Obst (pre epididymal)

↓

Rete testes obst.

↓

How to D̸ AZo

1. NL semen vol.
2. +ve fructose → Marker for seminal vesicle.
3. NL Biopsy

4. ass. serum anti sperm antibodies

why ??

↓

· 50% d.t Immune orchitis

(even if no Antibodies)

↓

ذي المحاولة يتم أخذ عينة ← اعرف إزاي

۳ - ۷ شهر

↓

50% show sperm +ve

- Few Cases → Natural Concept
- Most Cases → ICSI

Post or Extra testicular

↓

1. Epididymal
2. Vasal
3. Ejaculatory Duct Obst (EDO)

NB

· Epididymal & Rete testes — How to diff ??

↓

- ✓ NL Vol — Semen, Testes
- ✓ +ve Fructose
- ✓ NL Biopsy

+ +ve Markers

But

- Epididymal → ↓ α-glucosidase (in distal obst) · Vasography
- · Rete → ↑ antisperm Abs

(OA) Causes

- Rete testis (Intratesticular) → Immune orchitis — (4)
- Epididymal obst: · Cong · Traumatic · inflammatory · Neoplastic
- Vasal obst: · Cong · Traumatic · inflamm. — (3)
- Ejac. duct obst: · Cong · Traumatic — (2) AZo ↓ Semen Volume

Epididymal obst

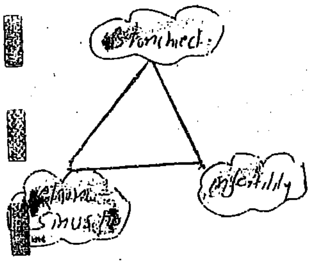
① Congenital:

- Failure of union bet. < body / tail / Vas
- Total tail aplasia (commonest)
- 2 Synd. ♀ (Y / CF)

Young (Azoospermia sino-pulm.) Synd.

↓

- No structural abnormalities but → thick Mucous sec. →
  1. obst of < VD / epidid.
  2. Lung → cough, sputum, sinusitis & bronchiect.
     ↓
     But no progression to pulm. damage as in (CF)



(قراءة)

Cystic fibrosis Synd.

Structural AbNL + Thick sec. ←

Affect:

- **Genital** (Wolffian) (Mesonephric duct derivatives) (Body - tail - Vas - SV - ED)
  1. CBAVD
  2. Epid. < Cauda / Corpus
     ↓
     NL Head (derived From...)
  3. absence or Hypoplasia of < SV / ej. ducts ←

  Bil. cong. Absent Vas

  ch: < Azo / ↓ Volume Semen

- **GIT** → Pancreatic exocrine Funct. defect (digestive enzs).
- **Renal** → any (CBAVD) → Renal anomalies (Ureter, UB, Kidney) — unilat renal aplasia
- **Respiratory**: thick obst. sec → pulm. impairment → RVF.

NB

- Caused by Mutat. in CFT Regulator Gene (CFRG) → play Role in: development of Mesonephric duct.
  cystic fibrosis trans-membrane conductor regulator gene
  ↑
  Thick rigid secretion

NB

- Typical operative findings in these anomalies
  1. Spermatocele (↑ mad)
  2. Missed epid. part → Replaced by Venous Conglomerate
  3. Remaining epid. parts → surr. by extensive Fat

  Fat ← الجزء الموجود
  Venous ← الجزء المفقود

NB : infertility ass. ē chest disorders

1. Young Synd
2. CF cystic fibrosis
3. Kartagener Synd (Immotile Cilia + Situs inversus)

② Traumatic:

[a] : accidental → Rare

[b] . Iatrogenic
- Test. Biopsy
- Epid. sperm Asp.
- ectomy
  - Varicolectomy
  - Spermatocelectomy
  - Hydrocelectomy.
  - Vasectomy.
    - ↑ intra epid. pressure → Granuloma & Fibrous tissue format → Obst.

③ Inflammatory (infect) (Epididymitis):

(A) Acute Infection : (< 6 ws)

C/p: Enlarged, S.f., Tender Epid. + Oligozoo.

Causative organism

< 35 ys.

1. organism < Chlamidia / N. Gonorrhoea
2. Route : usually Urethritis
3. Hx — Multiple partners; ± manif. of Urethritis.

> 35 ys

1. organism < E. Coli / Pseudomonas.
2. Route. bacteruria d.t Obst. urinary disord.
3. Hx
   - Prostate < itis / BPH / Catheter
   - UB infect / or obst.
   - Instrumentat.

(B) Chr. Epididymitis (> 6ws)

. C/p → Epid. Sclerosis & Atrophy

. organism → TB / leprosy

NB

Effect of TB on fertility: (20% of Pulm. TB → Extrapulm manifs esp. Genitourinary).

1. direct effect on Sperm
2. effect < Testis / Epid → tail & Post scrotal sinus. → obst.
Vas → beaded & obst

④ [redacted]:

either ← cystic
non cystic as ← Leiomyoma ✓
adenomas ✓
Rhabdomyo_Sarcoma ✓

→ Von Hipple Lindau synd ass. w:
✓ Cerebellar Hemangioblastoma
✓ Retinal "
✓ Renal_epididymal Tm (Cystadenomatoid Tm)
↓
Specific enough For ∅

Dd: Any bilat. epid. swelling → Put in mind this synd.

CF → Vas af obst

① Cong. → CAVD ± (CUAVD Unilat or Bilat (CBAVD)
Partial or Complete
Absence (or) atresia
Ass (as in CF)

- 1-2% of infertility
- 30% of Azoosp.

Cong. Absent VD

↓

abnormalities of:

- Epid. (Body, Tail)
- Vas
- SV
- ED. (Ejac. duct)

1. Genital
2. GIT
3. Renal (aplasia)
4. Respiratory

NB, Embryology

development

① Mesonephric duct (Wolffian duct) → epid (Bod, tail), Vas, SV, EJ-duct, Ureter

② Mesonephric Tubule → Epid: head

③ Testes → Genital ridge

② Traumatic < Vasectomy / Vasography / Herniotomy

Fibrous → Matted Vas

③ Inflamm. → Same as epid. as infect may spread from epid. to (Vas).

TB → Beaded Vas

Ejaculatory duct obst. (Rare)

Cong.

(1.) Failure of patency of Wolffian duct structures to become patent

(2) Persistence of incomplete Mullerian duct → female genital Tract structures presenting as obstructing cyst [middle line cyst at post wall of prostatic Urethra → (obst. the ejac. duct)] (Mullerian duct cyst)

Traumatic

(1) Transurethral surgery

(2) long term indwelling Catheterizat. cath

NB : Partial Obst.

(b) Testicular Biopsy may "quantatively" assessed & may diagnose Partial obst ?? depending on Correlat bet < spermatid score / tubule & Sperm Count / Ejaculate.

e.g Oligozoo (< 10 mil/ml) + > 20 Spermatid / Tubule → Partial Obst.

Diagnosis of Male duct Obst.

(1) History & clinical exam

(a). Testis → NL size (ē ...)

(b). Epididymis if obst → ē in epid.: < proximal to obst → Prominent (Full); distal half → empty.
→ at junct^n ē Vas or at the vas → dilated.

(c). Rectal exam → midline prostatic cyst ("Midline cyst" or Cat...)

(2) ... (Semen)

All Cases → (NL FSH) (ē ...) · NL Test. vol · NL Biopsy

(a) · picture of Rete obst → ; Epididymal obst →] "See NB"

(b) · " "

(c) · CBAVD & Ej. duct obst: عدم خروج → < SV. or ejac. duct

- ✓ [· ↓ vol · Azoospermia
- ✓ [· acidic PH · Failed Coagulation } (SV)
- Fructose & PGs → (SV markers)
- ✓ [· −ve epididymal markers: Carnitine, α-glucosidase, Glycerolphosphocholine

NB · unilat & Partial obst → difficult. { ·Vol ·Count ·Fructose } → all ↓ - Low NL

(3) Histopathology

· Bilat. open testicular Biopsy for evaluat of spermatogenosis should be done to exclude spermatogenic arrest before surgical intervention as in such case microsurgical reanastomosis unnecessary.

(4) Radiological:

(1) Scrotal U/S → allow direct imaging of testis, epid. & proximal part of Vas.

(2) Radiologic Approaches for ej. duct (or) vasal obst

- TRUS
- TRUS ē seminal vesicle Aspirat
- TRUS ē " vesiculography.
- " " seminal vesicle Chromotubat
- Vasography

---

(1) TRUS

Transrectal u/s —] ejac. duct obst 1st line of choice.

- indicat:
  - Hypospermia
  - Painful ejaculat
  - Hematospermia.

- Finding suggest Ej. duct obst:
  - ✓ Dilated SV > 1.5 cm width
  - ✓ dilated ej. duct > 2.3 mm
  - ✓ cyst, calcificat or stone along ejac. duct.

- not all cases of obst show dilated SV & not all cases of dilated SV are d.t obst — so do ↓

(2) TRUS ē S.V aspirat (Transrectally or perineally)

- +ve Finding if > 3 sperm / HPF
- لازم بعد فترة من القذف ٢٤ ساعة "

- disadv:
  - False +ve if prolonged Abst. > 24 hrs
  - Can't localize site of obst. — so do ↓

(3) TRUS ē S.Vesiculography:

- Retrograde study of SV & Vas
- dye injected into SVs ⟶ localize site of obst.
- but: More invasive > Aspirat.

④ TRUS ē SV Chromotubat:

بتحقن صبغة في SV ونلاقيها طلعت من الـ Ej duct ← prostatic urethra ē cystoscope لو مافيش انسداد. لو الصبغة متطلعش يبقى EDO

. Most accurate way for Ø

NB
. In study of 6 pts. ē TRUS → showed all have Ej. duct obst ∴ But → ē chromotubat only 3 obstructed

. used during TURED

⑤ Vasography:

. inj. of dye into vas to determine if there is physical obst at ← vas / SV / ej-ducts

. despite that TRUS is the 1st "line diagnostic procedure" in setting of ED obst

∴ "Vasography"
↓
✓ Remains the "gold standard" for diagnosis of ← pelvic / ing. / scrotal vasal obst.

. Method →
- antegrade (testes to prostate)
- retrograde (عكسي).
- Transrectal
- Trans perineal

① Clinical exam
② Lab invs
③ Radi ← U/S / vasal obst / EDO
④ Biopsy

Technique

- 3-4 cm upper scrotal incision is done → Testis is delivered & Vas separated from Spermatic Cord at junct & straight & convoluted portions → then → Remi transected (by micro knife under 15 Power magnificat) → then:

- Any Fluid coming from Vas is examined (if) Vasogram

① Nosperm in the Fluid → epid. obst.

② Sperm present → Vasal or epid obst.

③ Copious, white, thick Fluid & no sperms in a dilated Vas → Vasal & epid. obst.

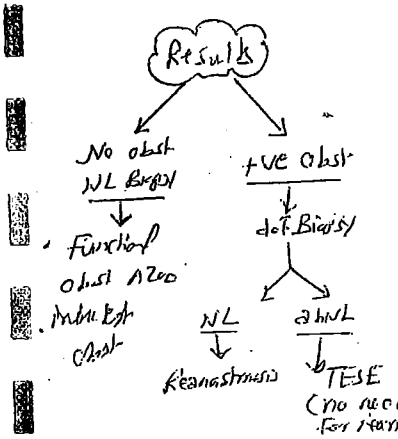
Then

angio Catheter is introduced into Abd. side & Vas → Gentle, low pressure in stillal & Saline or Ringer; if there is Easy Flow this means patency & requires no further Vasal study

- If there is Flow Resistance: this means obst & the level can be determined by introduct & urethral Catheter is introduced toward the S.V & inject (5% Conc & water Sol. Contrast media) Then

① If Vasogram shows ductal obst & NL testis → Test-Biopsy → Microsurgery

② No Obst, NL Biopsy & impaired emission → Sympathomimetics or electroejaculat.



• Complications:

① Inj. → stricture
② Infect^
③ Sperm granuloma
④ Retrograde inj of the mat. into epid → epid. injury.

⊙ Functional obstructive.

Azoo spermia

↓

d.t Sympathetic Injury or affect. (Sympatholytic)

caused by.

1. during operation (RLNO)
2. Diabetic neuropathy
3. Spinal Cord Injury (SCI)
4. Medications:
   - Tranquillizers
   - Anti Hypertensives
   - Anti depressants.

all ↓ peristaltic Movement of Vas &/or BN Neuropathy

↓

Failed emission &/or RGE.

(III) → Electro ejaculator (effective)

Azoospermia (10%)

absence of sperms in seminal plasma after repeated 3 samples after centrifugation

- Incid: 2-5% of infertility cases.
- to confirm it at least ≥ 2 centrifuged samples

- Classificat?:

Obstructive (OA)
- NL Testicular size (4-5cm)
- NL FSH
- NL Biopsy

↓ AET
- organic obst. → obstructive infert. (تتكلم عن) ↓ (Bilat/Complete Obs.)
- Functional obst.

Non obstructive (NOA) (Functional NOA)
- ↓ Testicular vol (ضمور)
- FSH ↑ or ↓
- AbNL. Biopsy

↓ AET

HypoGonadism (مرتفع)

Functional obstructive Azoospermia

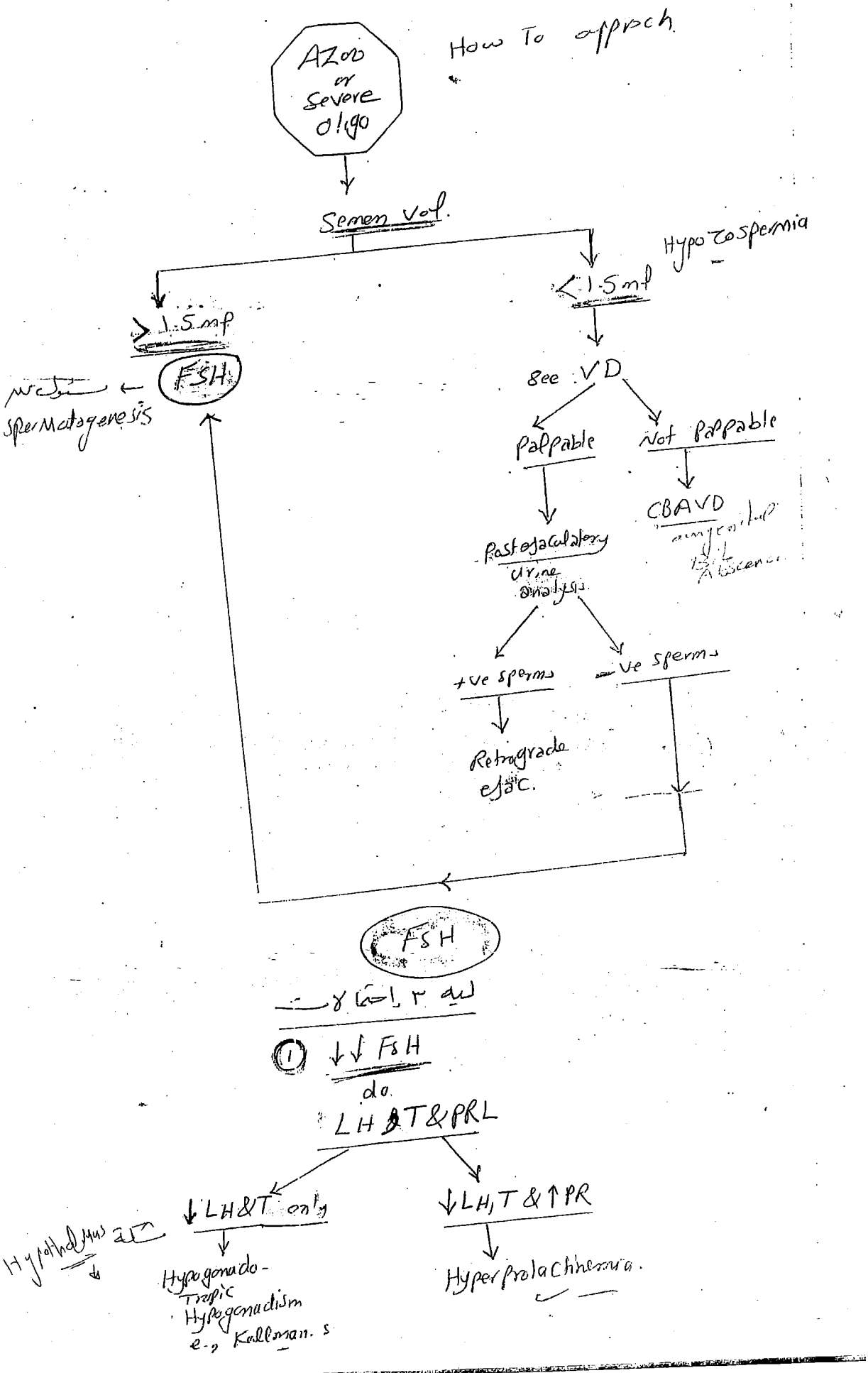
↓

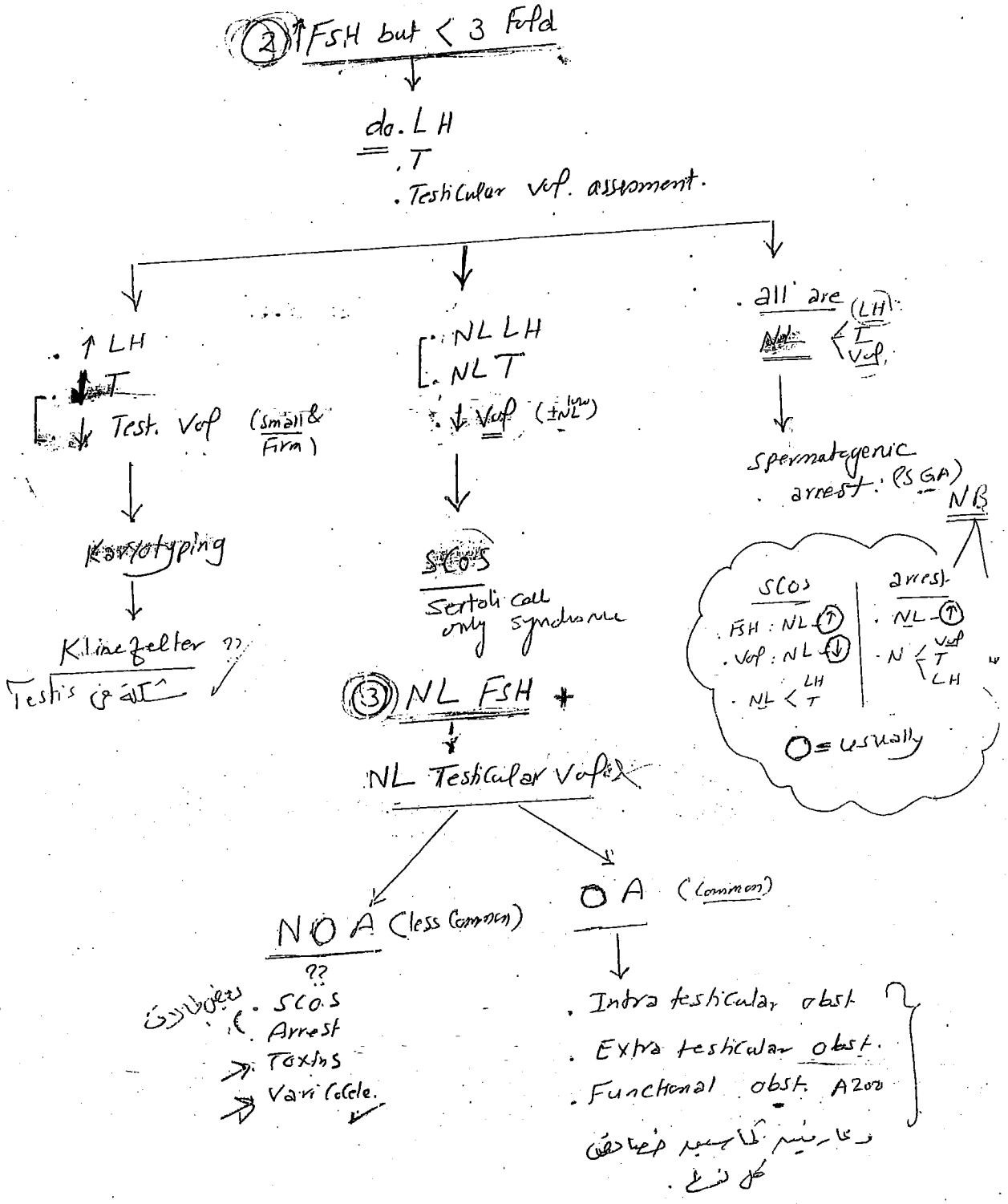
d.t. Sympathetic Injury or affect (Sympatholysis) caused by:

1. during operation (RLND)
2. Diabetic Neuropathy
3. Spinal Cord Injury (SCI)
4. Medications:
   - Tranquillizers
   - Anti Hypertensives
   - Antidepressants.

→ all ↓ peristaltic Movement of Vas &/or BN Neuropathy → Failed emission &/or RGE.

(H) → Electroejaculator (effective)


How To approch
Azoo or Severe Oligo
Semen vol.
Hypozospermia
< 1.5 ml
> 1.5 ml
FSH
Spermatogenesis
See VD
Palpable
Not palpable
CBAVD
Post ejaculatory urine analysis
+ve sperms
-ve sperms
Retrograde ejac.
FSH
↓↓ FSH
do.
LH & T & PRL
↓ LH & T only
↓ LH, T & ↑ PR
Hypothalamus
Hypogonado-Tropic Hypogonadism
e.g. Kallman's
Hyperprolactinemia.



للتفرقة بين النوعين

Vasography.

احتمالية نتيجة ال

Vasography

- **NL** → do Biopsy
  - **AbNL**
    - SCOS
    - Arrest
    - Toxins
    - Varicocele
  - **NL**
    - Rete testis obst
    - Sympathetic effects
- **AbNL** (obst of VD) → do Biopsy

Why ?? لازمة ايه ؟؟

- NL → Surgery
- AbNL → ICSI

④ ↑ FSH > 3 Fold

- Fresh Biopsy for ICSI
- or Adopt or AID

Treatment of ♂ ductal obst (OA)

① Preventive: avoidance & good th of infects

② Surgical:

- Vasoepididymostomy
- Vasovasostomy
- TU → damaging of Cyst
  - → RED (Transurethral Resect of Ejac. Duct)

in Cases of: Epididymal-vasal obst.

In Vasal obst.

③ ART → if failed surgery

✓

لازم

- CBAV → CFTR assessment & genetic Counseling.

Microsurgical VasoEpididymostomy

- **End - Side** (الأفضل)
  - in proximal & Mid epididymal obst. (obst. is easily seen ē dilated Tubules)
  - بنختار انبوبة متورمة في Epid. نفتحها وناخد في Vas نثبته في ال Tunica بتاع Epid. ونخيط طرفها
  - ال Vas + Mucosa of the single epid. Tube.

- **end to end** (Single Tubule anastmosis)
  - In distal epid. obst.
  - Suitable when
    - distal epid. obst
    - Short Vasal length.
  - بناخد cuts ابتداءً من ناحية Tail في Body لحد طلاع sperms ومبتخيطوش (نخيط في epid. Tubule داخل) ال Vas ونخيط
    - inner Vasal mucosa + outer Epid.
    - vasal Muscular layer + Epid. Tunica.

* Complications
  1. Hematoma
  2. Testicular injury & atrophy

* out Come:

Vaso-Epididymostomy
- Success Rate in Bilat. Cases
  - 50-80% of Cases → +Ve Sperms in Semen. (4 6ms)
  - 20-40 → Pregnancy (in 1st Y.)
- Caput obst → Poorer prognosis Than Caudal.

Vaso-Vasostomy
- Macrosurgical
  - Recanalizat.: 80%
  - Pregnancy: 40%
- Microsurgical
  - Recanalizat.: 90-100%
  - Pregnancy rate: 50%

Cystic fibrosis

Cystic fibrosis (also known as **CF** or **mucoviscidosis**) is a recessive genetic disease affecting most critically the lungs, and also the pancreas, liver, and intestine. It is characterized by abnormal transport of chloride and sodium across epithelium, leading to thick, viscous secretions.[1] → sweat, digestive juices, Mucus

CFTR → regulate Na & Cl Transport across epith of {sweat, mucus, digestive juices} → so impaired Fun'c of CFTR → Thick/Viscous

The name *cystic fibrosis* refers to the characteristic scarring (fibrosis) and cyst formation within the pancreas, first recognized in the 1930s.[2] Difficulty breathing is the most serious symptom and results from frequent lung infections that are treated with, though not cured by, antibiotics and other medications. Other symptoms, including sinus infections, poor growth, diarrhea, and infertility affect other parts of the body.

CF is caused by a mutation in the gene for the protein cystic fibrosis transmembrane conductance regulator (CFTR). This gene is required to regulate the components of sweat, digestive juices, and mucus.

There are two main populations of CAVD; the larger group is associated with cystic fibrosis and occurs because of a mutation in the CFTR gene,[1][2] while the smaller group (estimated between 10 and 40%) is associated with Unilateral Renal agenesis (URA). The genetic basis of this second group is not well understood.[3]

In the subset of males with both CBAVD and URA, the CFTF mutation has been shown to occur at a rate only slightly higher than the overall population. Thus, McCallum, et al. have suggested another mutation may be responsible for this condition.

Ht & Infertility → TESE & ICSI

So Any Case of CBAVD → CFTR genetic evaluat° → evaluat° of:

- Genital → absence or Hypoplasia of Wolffian duct structures
  - Epididymal ← Body tail
  - Seminal vesicles
  - Ejac. ducts
  - (97%)
- GIT → pancreatic Exocrine Funct° defect (digestive enz.) → Thick Visc. sec.
- Respiratory → Thick Mucus → obst → infect° → pulmonary Impairment → RVF
- Renal → Unilat renal aplasia (URA) → UTI, UIS

[CFTR has role in Wolffian duct development]

Infection & Infertility

- Genital Infection can be classified into:

① Orchitis.

② Duct System Inflamm. < urethritis / Epididymitis

④ MAGI (Male Accessory genital Tract inf.)

[Seminal Vesiculitis
[prostatitis.

Orchitis

- def: Acute inflammatory reaction of the testis (any) To an Infectious Agent; usually viral mumps.

- NB < Isolated Orchitis → usually Viral (sg. ↑) [Blood transmission]
  Epididymorchitis: → usually bact (acc. to the age).

Epidemiology

Mumps Parotitis

Prepubertal → rare Complicated by Orchitis

Postpubertal → 20% Complicated by orchitis (after 4-7 ds).
- 30% Bilat.
- 70% unilat.

Et < ++ Mumps (Paramyxovirus)
others
- Viral
- Bact.
- post Vaccinal
- Traumatic Surg.
- Irradiat.
- Autoimmune.

- 30% subclinical.
- 60% Infertility
- 7-13% Atrophy.

Causative organisms of orchitis

Viral
- usually Isolated orchitis
1. Commonest Mumps (Paramyxovirus)
2. less common:
   - Varicella
   - Echoviruses
   - IMN
   - Coxsackie.

(NB) Mumps Parotitis
- Prepuberal → rarely complicated By orchitis
- Post Puberal → 20% Complicated (3% Bilat., 70% unilat.)

clp: gradual onset of Symptoms (unilat in 90%)

Bacterial
- rarely Cause Isolated orchitis but usually Cause Epididymoorchitis
- * organism (See below)

Others
1. Post Vaccination
2. (viral) Immunocompromised ± d.t:
   1. MAIC
   2. Cryptococcus Neoformans
   3. Toxoplasma Gondi
   4. Candida Albicans
   5. Hemophilus Parainfluenza.
3. Irradiation & Autoimmune.

Clinical presentation

- Onset: 4–7 ds Following the parotitis.
- FAHM
- Testicular < Pain, Swelling
- Scrotum < Erythematous, Edematous.

- NB: orchitis ± Subclinical in 30–40% of cases.

Diagnosis (Invs) (Lab - Rad - Histopath.)

Back ↓ Epididymorchitis: (see below)

① Lab < Mumps → "IF antibody testing" "See"

② Imaging: → • Color Doppler US to Exclude Torsion → ↑ Perfusion.
• (Show inflamm. of Testis & Epididymis) → Non Homogenous or "Snow Flurries" picture

③ Histopathology:

. Severe interstitial Edema.
. Mononuclear cellular infilt.
. This reaction is enclosed in The Tough T. Albuginea → pressure Atrophy.

Complications:

① Reactive Hydrocele or Pyocele → ± Atrophy
② bil. Infertility (7-13%)
③ Atrophy (upto 60%).
7-13%

Treatment (Viral orchitis)

1. General Measures:

. Bed rest
. Scrotal Elevation
. Cold Fomentations

2 Medications:

. Vaccination
. Cs
. NSAIDs
. Interferon 2B
⊙ Early Incision & drainage of Hydrocele (to prevent Atrophy)

Epididymitis (Epididymo-Orchitis)

- def: inflammation of Epididymis usually (ω) may be acute (≤6 wks) or chronic. ← Bacterial & Ass. ē orchitis

- Pathophysiology: Epididymitis may be d.t:

Infectious

Prepubertal
may be d.t:

[1] Commensal: "E-Coli bacteruria"
(child ē recurrent Epididymo-orchitis
↓
Evaluate for UT Anomalies (50%)

[2]. Others
- Mycoplasma ✓
- Entro Viruses ✓
- Adenoviruses

Post pubertal
may be d.t:

① Age <35 Ys (Sexually active)
- N. Gonorrhoeae
- Chlamydia Trachomatis

② Age > 35 Ys (Elderly):
- commonly → Coliform bact. (E.C & K)
- less common → STDs CN. gonorrhoeae

Non Infectious.

① Chemical epididymitis: (d.t reflux & sterile uri

② Amiodarone (Antiarrythm

③ prostatic brachytherapy (Internal radiotherapy)

- Incid: Commenest Cause of infrascrotal Inflammat°
- Age: usually 20-40

- NB: Other Causes:
① Candidal (Immunocompromised)
② TB
③ BS
④ S.
⑤ leprosy.

Route of Inf.

1. Hematogenous
2. Retrograde from the Vas (d.t prostatitis or reflux of urine).

CIP

1. Gradual onset of flank & Abdominal Pain (vasal inflamm.) → descent to epididymis → Scrotal Symptoms
   - Scrotal < erythema, edema, pain
   - Epididymal < Edema, Tenderness ± < Fluctuation, Reactive Hydrocele
2. Prehn sign ?? & clinical Diff. from Torsion ??

Inv

- Urine < analysis, Culture
- Tests for N. Gonorrhoea & Chlamydia
- CRP, ESR
- Doppler

→ Torsion

Treatment

1. General Measures
   - as in orchitis.
2. Medications:
   1. Analgesics
   2. Antibiotics
      - prepubertal → Septrin
        - NB: Not effective against pseudomonas.
      - sexually active
        - Ceftriaxone 250–1000 IM
        - Doxy or Azithromycin

Prostatitis

- Def : Inflamm. of prostate.
- Incid : affect 50% of Men during certain Period of their life.
- Morbidity : Impair quality of life to the same degree as Coronary dis.
- NB : Zinc is anti bacterial factor in the prostate that prevent inf.

Classification Acc. to NIH (Recent)

- Type I : Acute bacterial prostatitis (ABP) ABP
- Type II : Chronic bacterial prostatitis. (CBP) CBP
- Type III : Chr. abacterial prostatitis (CNBP)
  (CNBP) = Chr. Pelvic Pain Synd (CPPS)
  Non.
  - 2 subtypes :
    - Type III A : Inflammatory CPPS
      (WBCs > 10/HPF in < EPS or Semen)
    - Type III B : Non inflammatory CPPS (Prostatodynia / prostatosis)
      (WBCs < 10/HPF in <)
- Type IV : Asymptomatic inflammatory prostatitis :
  Asymptomatic prostatitis with evidence of inflamm. in < Semen or Biopsy or EPS.

Acute & Chr. Bacterial prostatitis (Type I & II NIH)

- Incid : 5-10%.
- organism
  - < 35 yr (Sexually active) : → N. Gonorrhea & C. Trachomatis
  - > 35 yrs (Elderly) : → Coliform bacteria (Common of 80%):
    - E Coli
    - Klebsiella
    - Pseudomonas
    - proteus.

- Route of Inf:

1. Ascending : From urethra < STDs ; Gonorrh: & C.
   Instrumentation : as Staph
2. descending : From UTI or Bladder Inf. e.g. E. Coli
   d.t Intraprostatic urinary reflux : (objective)
   reflux of infected urine into prostatic ducts that drain the peripheral Zone because ducts positioned Horizontally.
3. Hematogenous: Septic Focus < Tonsillitis. Sinusitis.
4. Lymphogenous: From Rectum.

NB : Rare organisms as:

- MRSA (specially diabetics)
- TB
- Candida.
- Enterococci
- Anaerobes.

CIP

(ABP)

Symptoms

- Systemic S. FAHM
- Urinary Symptoms:
  - discharge.
  - dysuria
  - Frequency
  - Nocturia
  - ↓ Urine Flow
  - ± Retention.
- prostatic Symptoms: (Pain)
  - Perianal
  - penile tip
  - Ejaculatory
- prostatic Abscess:
  - Rectal Pain
  - Tenesmus
  - perineal discomfort.

Signs

(i) PIR → Tender, Nodular, Hot, boggy ± may be Soft & Fluctuate

(ii) Enlarged tender bladder: d.t urine retention.

Avoid Vigrous Message to avoid bacteremia & Septicemia

Invs

A. Lab:

- Urine: → ↑WBCs & +ve culture
- Eps: large No of ↑WBCs & Fat laden Macrophages.
- Blood Culture: may be +ve.

B. Rad CTRUS(CT)

X · Indications:

- inconclusive Lab.
- Poor response to ttt
- Suspecting complications. prostatic Abscess

CIP

(ABP)

Symptoms

- Systemic S. FAHM
- Urinary Symptoms:
  - : discharge.
  - : dysuria
  - . Frequency
  - . Nocturia
  - . ↓ Urine Flow
  - . ± Retention.
- prostatic Symptoms: (Pain)
  - : Perianal
  - . Penile tip
  - . Ejaculatory
- prostatic Abscess:
  - . Rectal pain
  - . Tenesmus
  - . Perineal discomfort.

Signs

(i) PIR → Tender, Nodular, Hot boggy ± may be Soft & Fluctuate

(ii) Enlarged tender bladder: d.t urine retention.

Avoid Vigorous Message to avoid bacteremia & Septicemia

Invs

A. Lab:

- Urine: → ↑WBCs & +ve culture
- Eps: large No of ↑WBCs & Fat laden Macrophages.
- Blood Culture: may be +ve.

B. Rad (TRUS & CT)

X · Indications:

- . inconclusive Lab.
- . Poor response to ttt
- . Suspecting complications. prostatic Abscess

ClP of CBP

① **Hall Mark:** Recurrent UTI; mostly ē the same pathogen ē "NL" UT Imaging.

② **Pelvic pain or discomfort:** Genito-pelvic "Aching"

"Pain" in the groin
- perineum
- buttocks
- lower abd.
- urethral

→ بيزيد مع القعدة الطويلة (العربية والسينما)

③ **Voiding Symptoms:**
- Frequency
- dysuria
- urgency
- ليل → Nocturia
- صبح → Morning drops → Small Mucopurulent drops squeezed from the Meatus at Morning or when urine Not passed for sometimes.
- stream < ↓ Force / bifurcate

④ **Sexual Symptoms:** < Painful ejaculat. / Hematospermia / PE. & ED (Impot.)

⑤ **P/R** → ± Some firmness (fibrosis from Chr. inf.)

شفوي

NB DD of Morning drops:
- CBP.
- Littritis
- Cowperitis
- Seminal vesiculitis
- Stricture Urethra.

Diagnosis of CBP

A. Lab: إختبارين

B. Rad.: TRUS & CT.

• Lab Ø of CBP ← بنعمله (3 cup test)

[A] Meares - Stamey 4 glass test: (1968)

• Collect urine from the patient as following:

- First 10 ml → تجمع Called VB1 (represent urine from urethra) هانرميه (descarded).
- Next 200 ml →
- Next 10 ml (midstream) → تجمع Called VB2 (represent urine UB).
- Then do: prostatic Massage → تجمعه (Called) EPS
- Finally: 10 ml of postmassage urine → تجمع Called VB3 (mix from P. Fluid & UB)

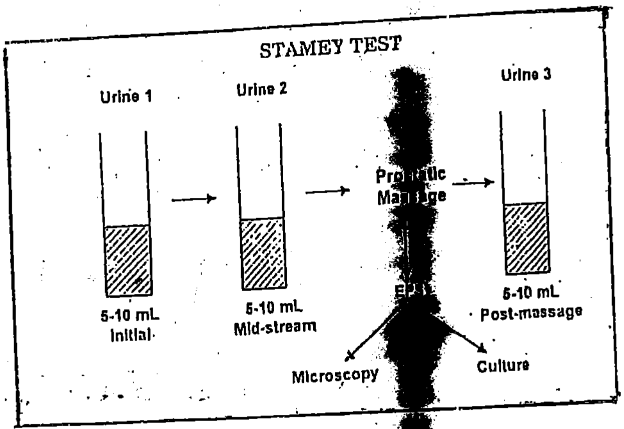
يعني EPS & VB3 نعملهم
1. Mic Exam for WBCs
2. Culture for bacteria

نتائج الاختبار

• ↑ Bact. in:
- VB1 → urethritis
- VB2 → cystitis..

• EPS & VB3: Look for WBCs / HPF (or Macrophage laden bodies)

- > 10 / HPF
  - ↓ do bacterial Culture
    - +ve (بشرط ان كمية البكتريا تبقى ١٠ أضعاف الموجودة (VB1 & 2 %
    - −ve → CNBP (III-A)
- < 10 / HPF
  - ↓ may be < prostate / other
  - • Prostatodynia (CNBP
  - • Urethritis
  - • Recent ejaculation



. disadv. of Stamey test:

1. difficult.
2. EPs difficult to be obtained
3. Impractical
4. Time consuming

علشان كده تم استبداله بالاختبار التالى ده

[B] Premassage & Post massage test (Nickel's Test 97)
(PPMT).

2 urine samples are obtained

→ Premassage sample (Pre-M)
→ Post massage sample (Post-M)

↓

Then send for:

1. Mic. Exam.
2. Culture

(as in Stamey)

NB

Patient c̄ chr. bacteriuria & -ve 4 cup test or PPMT refer to urologist for ??:

- Urine stasis
- Inf.
- Stones
- Abscesses
- Obst.

Prostatitis +ve if:

* WBCs:
  - -ve at preM & >10 at PM
  - 10x at prem but 10 times as NO in PM
  - or
  - -ve bact in pre-M & +ve in Post-M (or... as above

Treatment

(ABP)

1. Antibiotics
2. Analgesics
3. Antipyretics
4. laxatives.
5. Bed rest.
6. ↑ Fluid intake.
7. Complications ttt.

Oral (لفترة شهر أو شهرين..)

- Erythromycin
- Amoxycillin / Clavulinic a.
- TMP-SMZ
- Quinolones < Ofloxacin / Ciprofloxacin
- Ampicillin.

IV

- TMP-SMX
- Gentamycin + ampicillin

(CBP) ✓

1. Antibiotics
2. α-Blockers
3. NSAIDs
4. Hot baths. ✓
5. Message. ✓
6. TURP. ✓

ما تنساش إن شرط أي Antibiotic لازم يكون بيعدّي Prostatic barrier

الأفضل.

- TMP-SMX or
- Cipro.

لفترة ١-٢ شهر

ممكن كمان

- Ofloxin: جرعة ٢٠٠ مجم مرتين ..
- Levofloxacin: ٥٠٠ مجم مرة يومياً.

α-Blockers:

1. doxazosin (Cardura,
2. Tamsulosin (F

Selective α Blo
(A1) so:
- No Hypot.
- No need for
from initial d
- SE: F 1ac. dys

(dose) 0.4 - 0.8 mg

[B] α-Blockers: doxazosin (Cardura) in combinat° e fluroquinolones gives better results (symptoms relief & bact. eradicat°) than antibiotics alone.

[C] NSAIDs; Hot baths, Massage: may give some relief, but their role in bact. eradicat° (is) controversy.

[D] TURP (transurethral radical prostatectomy):

- it's a surgical resect° of all infected prostatic tissue
- Because, Most infect° is located in the peripheral zone of the gland, an extensive resect° of the gland is required to remove all infected & potentially infected tissue down to the level of the true capsule.
- More effective in patients e calculi.

Course & prognosis

- Longer courses are associated with better tt outcomes. (e.g. TG)
- Relapse is not uncommon.
- (tt) should be guided by urine culture results.
- If the first course of 4 wks failed → prolong the course, Best results are obtained with 12 wks course

Recurrent UTIs:

- may be associated e life threatening Septicemia.
- the cause of Relapsing UTIs are the poor penetrat° of most of antimicrobial agents or Bacterial sequestrat° (ie) protect bact. from antimicrobial exposure.
- only small ~~sized~~ Molecular sized unionized, Lipid soluble drugs that not firmly bound to plasma proteins are able to diffuse across the epithelial memb.

Chr. A Bacterial prostatitis (Non Bact) (Category III)

→ (CPPS)

def as before ← Pelvic pain or discomfort for at least 3 ms with Sexual & voiding Symptoms. (&/or) no demonstrated Inf.

Subtypes:

A (IIIA) → Inflammatory (CABP)

- WBCs in >10/HPF: Semen &/or EPS &/or Third stream bladder Specimen (VB3)
- (-ve Culture)
- "Si" Most Common Type of Prostatitis (90% of Cases)

B (IIIB) → Non Inflammatory CABP

- WBCs in <10/HPF: Semen &/or EPS &/or Third Bladder Specimen (VB3)
- Called Prostatodynia or Prostatosis or (CPPS)

Pathophysiology (Unknown but ± d.t)

Infectious

- Fastidious organisms that can't be cultured by routine Methods e.g
  1. Eact — ~~Ureaplasma~~ Chlamydia Ur.
  2. Fungal
  3. Viral
  4. Trichomonas

Non Infectious

(1) Autoimmune E.g Re
(2) Allergic
(3) Granulomatous
(4) Following
- CBP.
- TURP.

CIP: As CBP but differ in:

① PR < NL / < sensitive prostate / enlarged Boggy

② Course < Variable / More chr.

③ Psychologic stress → Exacerbation.

Diagnosis: ① Stamey test & PPMT:

- -ve Culture
- > 10 WBCs / HPF

② Other Invs: are Not practical, Time Consuming & Not diagnostic

So

A clinical approach is:

2-4 ws of Antibiotics

- Improvement → another 2-4 ws
- No improvement → Consider another AET
  - UTI
  - Cancer
  - SV anomalies
  - Ureteric Calculi

Treatment

4 lines

3 تعليمات

3:
- Fluids ✓
- Hot baths ✓
- # irritants : X
  - ش ش. — بهارات.
  - قهوة. — شيكولاتة.
  - الشيسه. — الكحوليات.
  - الكولا.

↓↓ pelvic floor Tension: 3

1. Diazepam
2. Manual self perineal Massage.
3. Frequent ejac. (/3ds)

3 Medications

1. Antibiotics
2. Anticholinergics
3. α Blockers

3 physiother

1. TUMT
2. Massage (prostatic)
3. Acupuncture

NB

- α Blockers
  - doxazosin (Cardura): 1 mg for 2ws then 2mg for 2ws then then asses or ↑ To 8 mg.
  - Tamsulosin (omnic): More selective & fewer S.E (0.3 - 0.8 mg)

TUMT (Transurethral Microwave Thermotherapy): (Effective 70%).

1. ↓ inflamm
2. ↓ pelvic floor Tension
3. damage the afferent Nerve fibs.

Prostatic Massage:

aim
1. Squeeze the clogged acini
2. ↓ size of gland
4. improve circulation.

- جلسه ٢-٣ مرات كل اسبوع
- بتتعمل ٢ لإدراك موقته
- دكتور عوزيس بتتعمل ... 20

Non Inflammatory CPBP
(Prostatodynia) = prostatosis.

. def → as before

. Aet: may be d.t

① Neuromuscular Mechanism:

. ext. urethral spasm (or) functional Obst → reflux of urine to the prostate

② BN in coordination.

③ Psychological disturbance e.g Anxiety

+. CIP ① discomfort & voiding symptoms

② Middle aged or young

③ Signs of anxiety, depression.

. Inv: ① Stamey test

② PSA → CBP ↑↑
Prostatodynia: NL

. Rx ① α Blockers ③ Anxiolytic.

② Massage

. Category IV: Asympt. inflamm. prostatitis.

. def: as before

. Rx: No Rx Except if:

✓ ↑PSA
✓ infertility
✓ Prophylaxis (before) Endoscopy

X . Ass. .qs: ē BPH
qu: ē Cancer

Effects of Inf. on fertility
(Mechanism of inf. induced infertility)

Effects of Epididymo-orchitis:

① Functional infertility: → d.t Testicular destruct & Atrophy

② Obstructive ~ : Epididymal inflamm. → Obst.

③ Immunological ~ : infect → Obst. → back pressure on Blood Testis barrier → Immunological infertility.

⑤ Ejaculatory infertility: urthritis → Stricture → back pressure on BN → Incompetence → RGE.

Effects of MAGI:

① Sperm damage & ↓ motility d.t
- attachment of Bact. to sperm tails.
- Clumping & Agglutination (BY E.)
- Release of Immobilizing Factor

② Sperm phagocytosis: Seminal Leukocytes
- phagocytose Sperms directly
- Release Lysosomal enzs → damage.

③ Accessory gland dysfunction:
- ↓ Vol
- ↑ Viscosity
- disturbed level of (Markers).

④ Generation of Inflammatory products & Immunological agents:

as
- ROS.
- Igs.
- Cytokines.

all
1. asthenozoo
2. Teratozoo.
3. ↓ sperm penetration
4. Obst. & Immunol.

Leukocytospermia

. Def.
. Diagnosis
... Effects → ROS

. HH

HH of Leukocytospermia

① Antibiotics
- . HH of inf. (Antibact)
- . ↓ Inflammatory Cytokines < IL_2, IL8, IL_4
- . ↓ ROS
- . ↓ Igs.

② Anti Cox-2 inhibitors.

③ Antioxidants. e.g. Carnitine.

④ Antihistamines e.g. Ketotifen → -- WBCs degranulation

Leukocytospermia

. Def.
. Diagnosis
. Effects → ROS

. Hx

Hx of Leukocytospermia

(1) Antibiotics
- Hx of inf. (Antibact)
- ↓ Inflammatory Cytokines (IL2, IL8, IL4)
- ↓ ROS
- ↓ Igs.

(2) Anti Cox-2 inhibitors.

(3) Antioxidants. e.g. Carnitine.

(4) Antihistamines e.g. Ketotifen → -- WBCs degranulation

Immunological Infertility

- def → Infertility caused by production of Anti-sperm antibodies.
- Incid: 4-15% of Infertility cases.
- Pathophysiology: (1) Sperm Antigens: < origin, Examples
  (2) Protective Mechanisms against Attack of sperm antigens
  (3) Anti-Sperm antibodies:
    - Site
    - classificat° < Ectopic, Biological
    - Titer
    - Causes of product°
    - Effects.

1. Sperm antigens:

- Origin: sperms are not present during Embryonic development when the Immune system develops "Tolerance" to self antigens
  ↓ so that
  sperm specific antigens (formed after puberty) are received as Foreign antigens by Immune System.
  Action: ضد المناعة against body cells.
- In addition: More antigens Acquired during < Their Test. development, Passage through epididym.
- Examples of these Ag:
  - CPK, LDH → Both regulate Spermatogenesis
  - FA-1 (Fertilizat° antigen-1): regulate (ZP) Interact°

2. Protective Mechanisms Against attack of Sperm antigens:

Immuno Separat^

- Sertolic cell → Blood Testicular barrier (Separate sperm Ags From Blood & Lymph → ??)
- Transformed growth factor Beta → TGF-β → Secreted from Sertoli cells & protect sperms from damage by antibodies inside the vagina.

Immuno-suppression (desensitization)

- There are (small gaps) in the B-T barrier that allow (small leaks) of sperm Antigens in to the blood → ++ suppressor T Cells → desensitizat^ (Suboptimum Antigenic stim. of Immune syst.)

Immuno paralysis

- CMI effectively paralyzed against sperms d.t Lack of both MHC-I & II required For CD8+ & CD4+ response (بالتركيب)

3. Anti-Sperm antibodies:

① Site:

- ♀: Serum, genital secretions
- ♂: Serum, Seminal fluid

∴ Serum anti-sperm antibodies have no Role in Infertility & Anti sperm antibodies are clinically important only if (they) are bound To The surface of spermatozoa → So (direct) testing For Sperm surface Antibodies is much more useful.

Type
Activity
titer

② Classificat^ : → (many Classifications) Acc. to:

ⓐ Isotopic ← IgM, IgG, IgA (more potent)

- Serum → Ig G & M
- Fem. & male genital sec → Ig G & Ig A.

penetration
interaction ⟩ فالتالي اتبع

ⓑ Biological Activity ← تأثيرهم على إجراء السرعة

[i] Coating Igs → Membrane defects → ↓ ATP & cot → Asthenc. also ⟨ ↓ Cx penet. ZP AR

يلزق sperm مع بعض ← [ii]. Agglutinating

Asth. ← [iii]. Cytotoxic or Immobilizing.

NB: Pattern of ⟨ Coating: ± to ⟨ Head, mid piece, principal tail (tail tip) No signific. ; autoagglutin.: H-H, H-T, T-T (Tail tip)

NB: IgM is present in the serum & doesn't pass to the male genital tract (d.t large size)

So Ig ⟨ G, A → responsible for Immunological Infertility

IgA (secretory)	IgG
. potent . ass. ē Idiopathic & ± inf. Induced Antisperm antibs	. weak . ass. with obst. Azoo & vasectomy ass antisperm antibs.

So Immunological infertility usually d.t (IgA > IgG)

مهم ③. Titer:

	Serum titer	Seminal fluid titer
° Insignificant effect	≤ 1:32	—
. Marked reduction of fertility	1:64 - 1:512	≤ 1:16
. Sterility	> 1:512	≥ 1:32

NB → The presence of Agglutinating Antibodies in seminal fluid → worsens the prognosis.

④ Causes of Production of Anti-Sperm antibodies: (All → d.t disturbed barrier)

① Cong < genital ductal obst. (...) / Cryptorchidism

② Traumatic < Trauma. / Torsion. / Biopsy. / Vasectomy → leakage d.t barrier disruption

③ Inflammatory < Epididymoorchitis / prostatitis — may → direct barrier affects - or via obst.

④ Neoplastic → Testicular Tm (ex Mchanism).

⑤ Varicocele.

⑥ Idiopathic.

⑦ Recipient Homosexuals.

⑧ Genetic < Thymic Mal development / HLA-B 28 ✓

NB
- Mumps orchitis may → Contralat. orchiopathy
- unilat. Test. obst ± → oligo. through Contralat orchitis.

↓

By exam:

- affected one (orchitis) → Smaller (defective Spermatogenesis)
- Contralat one ⟷ NL size, Soft, Swollen epid.

- Soc. of Vasectomized Men: have antisperm antibodies; So before Vasovasostomy do → titer for Antibodies; if (Higher) → low chance of Conception

Diagnosis of Immunological Infertility

Indications For doing Immunological Invs.

1. Marked Sperm agglutination (>10-15%)
2. Leukocytospermia >1 million
3. ~~post coital test~~
   - If poor
   - If shaking movement
4. unexplained Isolated Asthenia
5. unexplained infertility + (recurrent) abortion despite NL Semen.
6. Vasectomized Men
   - prior to Vasovasostomy

Types of Immunological Invs

Invs for:

- detection of Antisperm antibodies
  - ① Immuno bead Test
  - ③ MAR Test
- detection of effects of Antisperm antibodies
  - ① Sperm-mucous Interact^ Test.
  - ② Sperm capacitat^
  - ③ Zona-binding & Acrosome-React^

Find indicat^ for doing Invs → Inv. For detect it → Investigate for its effect

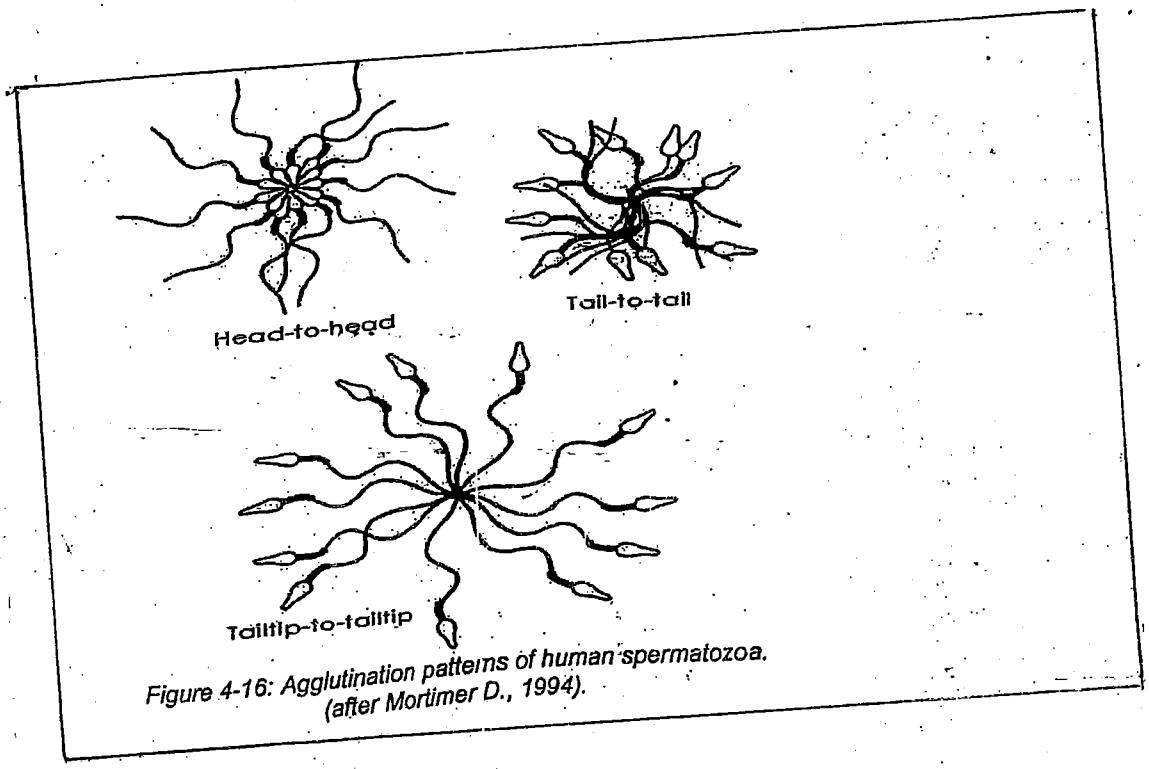


Figure 4-16: Agglutination patterns of human spermatozoa. (after Mortimer D., 1994).

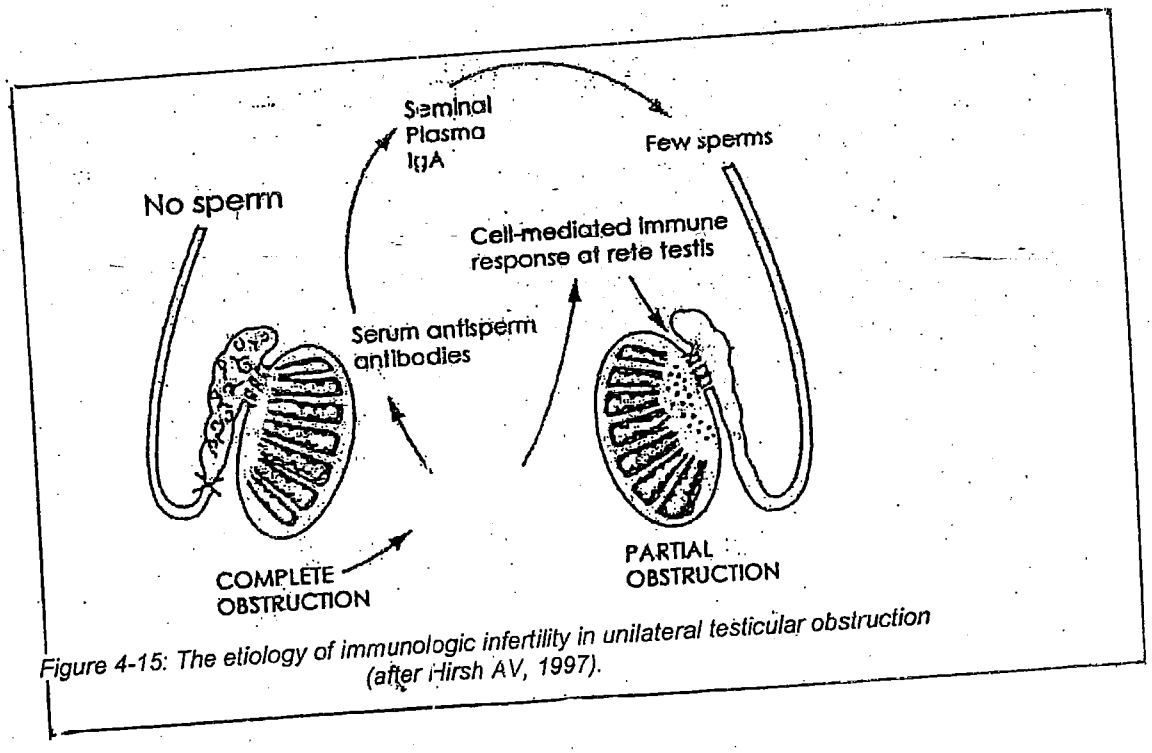


Figure 4-15: The etiology of immunologic infertility in unilateral testicular obstruction (after Hirsh AV, 1997).

⑤ Effects of Anti-sperm antibodies.

- On sperm Transport.
  - Astheno. (Coating)
  - Autoagglutinat⁻
  - Immobilizat⁻
  - destruction (Cytotoxic)
  - Impaired Cervical Mucous penetrat⁻ (post coital test)
    - ↓
    - shaking Movement (only) or Immobilizat⁻
- Sperm-ovum Interact⁻
  - Inhibition of
    - Sperm capacitat⁻
    - Zona-binding
    - AR
- Embryo development
  - Inhibition of cell division & cleavage of Fertilized ovum.
  - Direct act⁻ in developing Embryo. eg Abortion.

- Pattern of Agglutination
  - Pattern
    - H-H
    - H-T
    - T-T

(Coating)

- Pattern of Coating & its effects:
  1. ∂ Head → No AR & ovum penetrat⁻
  2. H & mid piece → Failed Cervical Mucous Penetrat⁻
  3. End tail piece → Insignificant.

Treatment of Immunological Infertility

(1.) prophylactic Rx : Rx of the cause < Inf. / Obst.

(2) Curative Rx : → Immuno suppression BY Cs
طريقتين ✓

High dose Cyclic therapy

١٢ قرص هيدروكورتيزون (أو بريدنيزولون) (أو) أوربازون يومياً لمدة ١ أسبوع
من كل شهر (15th - 21th day of Cycle)
✓ لمدة ٢ شهور.

Urbazone = Methylprednisolone (tab = 8 mg)

↓

Other Regimens

. أول ١٠ أيام ٣ دورة ← ٨ أقراص هيدروكورتيزون
. ليوميه ١١، ١٢ ← قرص مرة
[٣ شهور]

Intermediate dose Continous Therapy

. 15 - 40 mg / d prednisolone for 9 ms.

(3.) ART < IUI / ICSI (Most effective).

15-40 mg/d

Infertility d.t Environmental Gonadotoxins

A. Environmental Gonadotoxins

B. Targets of Toxicity

[A] Environmental Gonadotoxins

(Examples of occupational Exposures).

(1) Ionizing radiation

- Source: - Accidental: (atomic bomb) قنبلة ذرية
  - occupational الاشعاعيون
  - Therapeutic.
- Effects acc. to the dose: ← Spermatogenic damage / Mutation

- Reversible spermatogenic damage:
  - 20 cGy → ↓ Sperm Count
  - 75 cGy → Azoospermia.

cGy ↓ "rentigray"

[A] damage

- Irreversible damage: doses upto > 400 cGy

[B] Mutations & chromosomal damage.

(2) Anticancer therapies ← X-radiation & Cytotoxics

الكيماوي. الاشعاع.

- Effects → Genetic damage of Germinal stem cells
  → Malformations & / or Transmission of Mutations.

(3) Dibromo chloropropane (DBCP)

يستخدم لمكافحة آفات النباتات زراعية وإنتاجية.

. Effects: reversible or irreversible testicular damage → oligo ⇒ Azoo ↑ FSH & LH.

(4) Complex organo-chlorine Compounds (Endocrine disrupters)

مركبات الكلور العضوية

. Endocrine disrupters: are Chemical Compounds That Have { Estrogenic / Anti " / Anti-androgenic } Hormonal Effects.

. Estrogenic activity called [Xenoestrogens] →

prenatal exposure → -- fetal testicular development

→ Infertility.

(5) Smoking

. Contain Many harmful Compounds e.g. Acrolein

. Effects: (1) DNA damage (chromatin disturbances, DNA adducts in sperm & Embryo).

(2) Failed ART.

(3) ↓ Semen quality.

(4) Cryptorchidism. في الخصيتين

(6) life style Factors:

1- Cell-phones: الموجات الكهرومغناطيسية بمادة البلاستيك المحمول ممكن تقلل OAT

2. Testicular Hyperthermia: Hot tubs, Jacuzzis & Lap tops. → ↓ sperm parameters

(7) Alcohol & illicit drugs

- Alcohol → (1) ED, libido, Gynecomastia
  - (2) -- HPG axis
  - (3) ++ T aromatization → ↑ Estrogen.
  - (4) ↓ antioxidants → oxidative stress.

- Marijuana : OAT
- مورفين - Opiates : ↓ GnRH / ED
- Cocaine : ED
- Amphetamines : ↓ libido.

B Mechanism or Targets of Toxicity

1. pretesticular

التعرض للمركبات الاستروجينية كما في صناعة حبوب منع الحمل أو التعامل وملامسة بعض المواد الكيميائية كذلك

Non-steroidal Estrogen.

↓

-- FSH & LH sec.

2. Testicular

↓ the 3 types of cells ± affected.

(1) Sertoli Cells: → impaired Spermatogenesis.

3 types of industrial chemicals have been implicated as: Sertoli Cell Toxicants:

1. phthalates (for plasticizers)
2. Nitro-aromatic Compounds :
3. γ- Ketones: a Solvents

3. post testicular

(i) epididymal
- lytic
- arrest
- Toxic
- Necr

(ii)

1. Cyclophosphamide: preimplantation loss after Fertilization

2. Epididymis affect

(i) Adrenolytic drugs → stasis of Sperm inside epid. e.g. guanethidine (Anti HTN)

(ii) Accelerated Transport → Immature sper.

(iii) Epith. Toxins : Gossypol
- AIDS 2.ve
- Cancer
- Contraceptive ♂
- ♀ : endometriosis

(3) prophylactic Cryopreservat: (لأ ؟ ليه)

(4) if pt able to conceive Naturally — (d/t ↑ incid. of Chromosomal or Cong. anomalies).

(5) TESE (45% success).

- Hormones & Hormonal agonists: all -- pituitary

Testosterone
- → Exogenous TRT
  - ↓ -- Axis ??
  - إزاي تعالجه لحد ما يوقف T ؟؟ → (hCG)
- → Anti Test. drugs
  - opiates: -- LH
  - Ketoconazole: -- enzymes product
  - barbiturates: ↑ metabolism
  - -- Rs: Aldactone & Cyproterone A.

NB Anabolic Steroids:
لو أخدها جرعة أكتر ٤٠ مرة من المسموح بيها
احتمال يحدث تسمم للخصية لحد توقف العلاج ٦-١٢ ش

(Antiandrogen & Androgen inhibitors)

Surgical Iatrogenic infertility

(1) Any surgical procedure (sp. if ē GA) is followed by suppression of spermatogenesis which lasts for (3-6 ms).

(2) Epididymal obst ± d.t: Test. Biopsy, Varicocelectomy, Hydrocelectomy, Spermatocelectomy

(3) Vasal obst: vasectomy, vasography

(4) EDO: urethral catheterizat → inf. → obst.

(5) Urethral obst. & Stricture: urethral catheterizat → pooling of ejaculate to flaccid segment of urethra

(6) BN Incompetence: BN reconstruct (...) & RPLND ?? → AGE.

→ RPLND → Anejaculat

(1) Spermatogonial Cells :

. Ac or stem Cell
Toxins e.g Chemo-therapy < Nitrogen Mustard / Vincristin

↓

. Irreversible damage .

Sp... ...ment ... sensitive ...luminal ...cells

. proliferating Spermatogonia (B)
more sensitive to cytotoxic effects of chemoth. → (Complete) but temporary loss of spermatogenesis
(as they are replaced By stem cell prolif.)

(3) Spermatocytes :

± < damaged / Genetic Mat.

e.g Methoxy ethanol

ع لماذا

[Spermatocyte toxins]

مريض ← مثال
نقاش إشائون

(3) Epididymal Necro-Spermia Synd. :

ornidazole may cause loss of sperm motility

...sure	Effects on
Heat	Sperm morphology, motility, fertility
Radiation	
X-rays	Sperm count, mini satellite mutations, fertility?
Heavy metals	
Lead	Sperm morphology, count, motility, semen volume, fertility?
Synthetic estro...	
Diethylstilbo...ol	Hormone levels, genital malformations
Oral contrac...es	Gynecomastia, libido, impotence
Glycol ethers	
2-Methoxy-...nol	Sperm morphology, count
2-Ethoxy-eth...ol	Sperm morphology, count
Pesticides	
Dibromo-chl...propane	Sperm count, motility, fertility
Ethylene-dib...mide	Sperm morphology, count, motility
Solvents	
Carbon disul...de	Sperm morphology, count, impotence

Iatrogenic Infertility

Def. Medically (drug) or Surgically induced infertility.

Causes

A. Medical (Drug induced)

B. Surgical

Table 48.1: Drugs with possible influence on male fertility.

Suppression of spermatogenesis

1. Cytostatic agents (Drugs that ... Cell division)
2. Hormones and hormonally active drugs: androgens, anti-androgens, oestrogens, progestogens, glucocorticoids, anabolics, cimetidine, spironolactone, digoxin, ketoconazole.
3. Psychotropic drugs, antiepileptics, antiemetics, analgesics, certain antibiotics and chemotherapeutics, anthelmintics such as niridazole, salazo-sulphapyridine

Impairment of sperm function

Calcium channel blockers (sperm motility and sperm-egg binding)
Antiepileptics (sperm motility)
Sulphasalazine (sperm count and motility)
Antibiotics (sperm motility)
Amantadine and colchicine (Sperm-egg interaction)
Psychotropic drugs (SSRIs and tricyclics) alpha- and beta-blockers (sperm motility)
Cyclosporine (sperm motility)

Inhibition of sperm transport (Sympatholytic = adrenolytics)

Antihypertensive drugs
Psychotropic drugs

NB

(1) Cytostatic = Chemotherapy

- Type B Spermatogonia are the most affected (Most Proliferate Actively)
- incid is high ē Alkylating agents : Cyclophosphamide & Chlorambucil
  - low ē others : MT, prednisone & Vinblastin.
- Hx of chemotherapy induced infertility:
  1. Combinat° Chemotherapy : lower doses → ↓ damage.
  2. Prophylactic Hormonal Hx : GnRH agonist or antagonist → Stop Spermatogenesis during Chemoth. → allow survival of Spermatogonia to differentiate after therapy.

(8) Hernial repair: → obstructive infertility (Vas or epid. obst)

(9) Vasectomy: → Most common cause of Obst. infertility
→ ± → Immunologic infertility.

رضع كلية عزل
Irradiat

- Diagnosis
  - Hx
  - Exam
  - Invs
- Rx: to the cause.

---

(1)

Hypogonadism

. Def. Testicular Hypofunction ch BY impairment of one or Both of testicular Functions (T. Sec. & Spermatogenesis)

↓

< 10.5 nmoles/l < 365 ng/dl → Diagnosis of Hypog.

. Types (Classification):

(i). Acc. to the Etiology:
- 1ry Hypogonadism (Testicular or Hypergonadotropic)
- 2ry " (Pretesticular or Hypogonadotropic)
- Others: Mixed & Normogonadotropic Normogonadism (Idiopathic)

(ii). According to the onset:
- Cong.
- Acquired (late onset)

. CIP: depend on time of onset of Testicular Impairment

① Fetal Hypogonadism (Very early onset Hypog.) [V EOH]

(XY) ♀ Female genit.
↓
No menses
↓
يرجع يكشف
↓
يطلع
Male.

d.t ↓ T. Sec. or defective act during the 1st Trimester usually d.t Androgen insensitivity Synd (AIS): (XY)
- Female or Female genitalia
- Ambiguous genitalia.

. presentation:
- غالبا يرجع لما يبلغ او يتزوج
- تتأخر: Amenorrhea او يتزوج
- Inj. Hernia. جراحة تتأخر عملية زايدة

② Prepubertal & Peripubertal Hypogonadism:
- Prepubertal → ست صبيان ما اعراض البلوغ
- Peripubertal → partial/Complete lack of virilization.

③ Adult Hypogonadism e.g. in Men ♂ Past History of (NL fertility & NL virilization) usually pituit. Macroadenoma or Haemochromat
- Gynecomastia
- ↓ libido → ED
- ↓ Test. vol, Semen vol, Prostate size.

(HL) NB What is the Androtest: in pt. ē sexual dysf.

a 12 items structured interview providing score useful for detecting hypogonadism has been recently developed (EAU) [248]

[illegible]

(4) Late onset Hypogonadism (LOH): = "Mixed hypo & Hypergonadotropic Hypogonadism = Andropause.

mid NL LH ē ↓ T level.

2ry Hypog. + T [illegible] Pituit. [illegible] > Nipple [illegible]

[illegible] عدم استجابة الخصية لـ LH [illegible]

↓ 1ry Hypogonadism.

LOH = Andropause (Male Climacterium) = ADAM (Androgen deficiency in aging men) = PADAM (Partial)

[illegible]
Menopause [illegible]
chBI < Abrupt & Complete
. Ovarian Funct. in ♀.

PADAM = Andropause [illegible]

. Def. Ageing related gradual decline in Test. level.

. Etiology . (1) Endocrinal either d.t < Hypothalamic-pituit. Hypof. [illegible] / Testicular dysf. [or Both = Mixed].

(2) ↑ SHBG.

. Onset: gradual ↓ Start at 35-40 Y. & onwards. (40-70) & at 50Y → 30%.

. Premature Andropause (Est) [illegible]
. Pharmaceuticals.
. Plastics & pesticides
. Near Incinerators.

. By Mid 50th → 30% experience Andropause.

. Risky pt. (1) obese (2) D.M (3) HTN. (4) Genetics (K.S, AIS) [Klinefelter]

[illegible] Metabolic or Vascular Complications

Diagnosis of Hypogonadism

(1) History (↓ libido, ED, Poor beard growth, Anosmia ??)
↓ أهم سؤال في حالة (Cong. Hypogonadism)

→ Specific S:

Non Specific S:
- ↓ Ms mass & Strength
- ↑ body fat
- Osteoporosis
- low energy
- depression
- ↓ Vitality.

(2) Exam → Signs of Eunuchoidism.

(3) INVs → Endocrine (F) / Spermatogenic (F)
3. Genetic assessment
4. Imaging

(a) T. level
NL. Total 10 - 35 nmoles/L (300 - 1000 ng/dl)

Calculated Free T (No Consensus about low level): lower limits are: 300-150 Pmols/L.

(b) LH

(c) PRL: if T is low + NL/low LH → asses LH.

(d) GnRH ++ test

متى نستخدم → (e) hCG stim. test: . 1000-2000 IU/d . for 2-3 ds
نستخدم ؟؟

(f) Semen (g) FSH & Inhibin.

· Genetic assessment:
① WBCs Karyotyping : → K.S
· CFTR ; Kallman S (Kal1), IHH, PORK2

· Imaging: → U/S : Testicular & epididymal & varicocele
→ MRI for CT on Pituit.

(Testis) - Size - T... + Micro Calcific. (Micro-lithiasis)